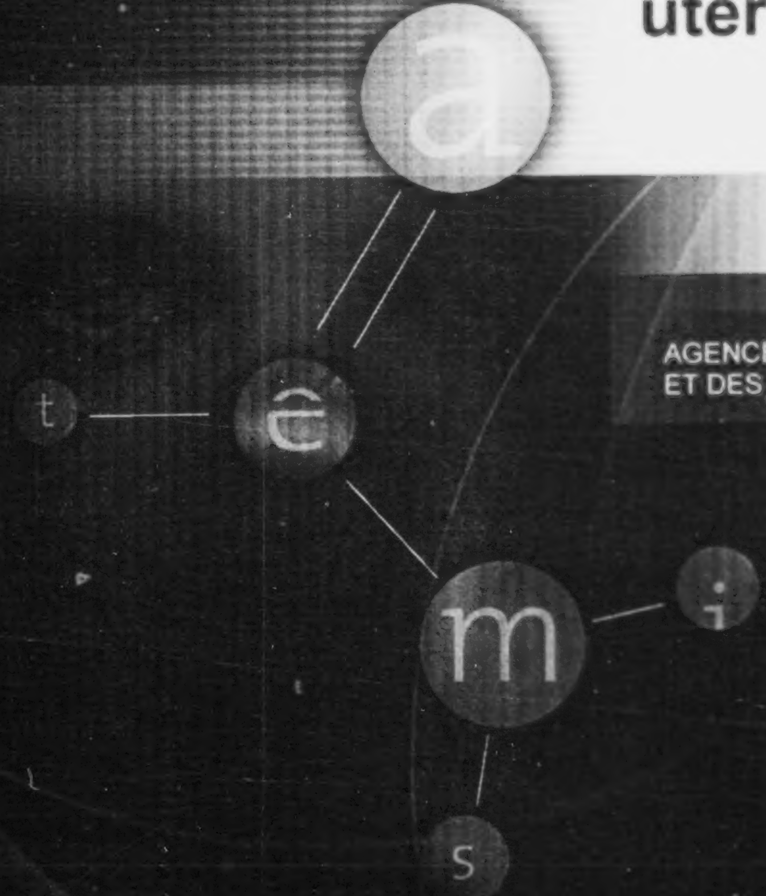
Endometrial ablation techniques in the treatment of dysfunctional uterine bleeding



AGENCE D'ÉVALUATION DES TECHNOLOGIES
ET DES MODES D'INTERVENTION EN SANTÉ

Québec

Endometrial ablation techniques in the treatment of dysfunctional uterine bleeding

Report prepared for AETMIS by Chantale Lessard and Alicia Framarin

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FOREWORD

ENDOMETRIAL ABLATION TECHNIQUES IN THE TREATMENT OF DYSFUNCTIONAL UTERINE BLEEDING

Dysfunctional uterine bleeding (DUB) is a deviation, from the normal pattern, in the frequency of menstruation or in the duration or amount of bleeding, in the absence of pregnancy, an infection, a tumor or some other organic lesion. Its prevalence is reportedly 20% worldwide and is even higher during adolescence and the decade preceding menopause. Dysfunctional uterine bleeding and menstrual pain (dysmenorrhea) account for one-sixth of the hysterectomies performed in Québec and are the second leading reason for undergoing this procedure. Although hysterectomy is a definitive treatment for these conditions, it is a major surgical procedure with inherent risks and the potential for complications. This is why endometrial ablation was adopted, toward the end of the 1980s, as a less invasive option and has already undergone different changes aimed at making it easier to perform.

This report, which is in response to an assessment request from the ministère de la Santé et des Services sociaux, examines the efficacy, safety and acceptability of the different endometrial ablation techniques, specifying the status, in terms of technological evolution, to which each technique has advanced for broader diffusion. The report also looks at the health-care costs associated with the surgical treatment of dysfunctional uterine bleeding.

Nine techniques were examined. Three of them–transcervical resection of the endometrium, rollerball endometrial ablation and thermal balloon endometrial ablation–are considered accepted; another, endometrial laser intrauterine thermotherapy, is experimental; and ordinary laser ablation is no longer performed in Québec. The other four techniques receive innovative status: microwave endometrial ablation, hydrothermal endometrial ablation, endometrial cryoablation and impedance-controlled endometrial ablation. Innovative techniques should be used only in settings where the clinical outcomes can be evaluated on an ongoing basis and where, if the techniques are diffused more widely, possible training requirements can be determined.

Apart from the aspects of efficacy, safety and efficiency, women's expectations and preferences, the possibility of earlier management of dysfunctional uterine bleeding, and the organizational and economic repercussions are issues that should be explored for optimal utilization. Thus, the repercussions of endometrial ablation techniques and therefore the role of these techniques in the treatment of dysfunctional uterine bleeding cannot be fully determined until after a long-term follow-up. Lastly, this report recommends that the assessment be updated on a regular basis, given the rapid technological evolution of endometrial ablation.

In disseminating this report, the Agency wishes to provide the best possible information to the decision-makers in Québec's health-care system concerned by this important matter.

Renaldo N. Battista
President and Chief Executive Officer

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The Agency also wishes to recognize the external reviewers for their numerous comments, which improved the quality and content of this report.

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Lastly, the Agency wishes to express its gratitude to the different companies that generously provided information on the endometrial ablation devices examined in this report.

SUMMARY

Current situation

The primary treatment of dysfunctional uterine bleeding is usually medical. When drug therapy fails, surgical intervention is often the next option. Hysterectomy has, for a long time, been the definitive treatment for dysfunctional uterine bleeding. Dysfunctional uterine bleeding and menstrual pain (dysmenorrhea) were the main indication for 16.2% of the hysterectomies performed in Québec in 1996-1997 and the second leading reason for undergoing this procedure. However, hysterectomy is a major surgical procedure with inherent risks and the potential for complications.

Endometrial ablation was adopted in clinical practice toward the end of the 1980s as a less invasive alternative to hysterectomy for dysfunctional uterine bleeding. This surgical procedure permits preservation of the uterus and reduces uterine bleeding in most patients. The first-generation ablation techniques are based on the use of laser or electrosurgical techniques and are aimed at destroying the entire thickness of the endometrium. All of these techniques are hysteroscopically assisted, with direct, real-time visual monitoring of the uterine cavity.

Although the first-generation endometrial ablation techniques are clearly effective, too little use is still made of them in certain cases, largely because of the need for specialized training and the fear of surgical complications. This explains the efforts to develop most of the new endometrial ablation techniques. These second-generation techniques are designed to destroy the entire thickness of the endometrium while at the same time preventing the associated risks and obviating the skill requirements that the first-generation techniques entailed. In fact, the majority of these new surgical techniques do not require hysteroscopy. Most of the second-generation techniques are available in Canada, including microwave ablation, which is presently being tested.

Objective

In the fall of 2000, the ministère de la Santé et des Services sociaux du Québec submitted an assessment request to the Agence d'évaluation des technologies et des modes d'intervention en santé, asking it to define the role of microwave endometrial ablation in the treatment of dysfunctional uterine bleeding.

This assessment report mainly concerns the efficacy, safety and acceptability of microwave endometrial ablation and compares this technique with transcervical resection of the endometrium, which is the procedure currently performed in Québec hospitals. However, a decision was made to broaden the scope of this report in order to document the situation in Québec regarding the practice of endometrial ablation in the surgical treatment of dysfunctional uterine bleeding. Consequently, the report examines the specific status of each technique in accordance with the classification developed by the Agency: experimental, innovative and accepted status. Secondly, the report looks at the health-care costs associated with the surgical treatment of dysfunctional uterine bleeding.

Dysfunctional uterine bleeding

Dysfunctional uterine bleeding is a deviation, from the normal pattern, in the frequency of menstruation or in the duration or amount of bleeding, in the absence of pregnancy, an infection, a tumor or some other organic lesion. Its prevalence is reportedly 20% worldwide and is even higher during adolescence and the decade preceding menopause.

The most frequent cause of dysfunctional uterine bleeding is anovulation. The exact proportion of cases of dysfunctional uterine bleeding in the presence of ovulation is apparently very low. In the West, dysfunctional uterine bleeding is the leading cause of iron deficiency anemia. The alkaline hematin test (hemoglobin assessment) is an objective method for measuring excessive menstrual bleeding. To a certain extent, a diagnosis of dysfunctional uterine bleeding is made through a process of elimination. It is therefore essential to look for the cause of the bleeding before undertaking any treatment.

Treatment of dysfunctional uterine bleeding

The objective of treatment is twofold: to eliminate excessive bleeding and to improve the patient's quality of life. Dysfunctional uterine bleeding should be considered an endocrine disorder that is best treated first medically, the more invasive forms of treatment being reserved for refractory cases.

Medical treatment

Hormone therapy is the basis of treatment, since, in most cases, the underlying cause of dysfunctional uterine bleeding is anovulation. In the absence of a causal disease in a woman who ovulates and who has dysfunctional uterine bleeding, consideration should be given to using nonsteroidal antiinflammatories (NSAIDs) or antifibrinolytics on a first-line basis. Danazol and gonadotropin-releasing hormone analogs are two options used in the treatment of menstrual bleeding refractory to the other forms of therapy.

Surgical treatment

Curettage stabilizes bleeding in some women, but its effects are almost never long-lasting. This procedure is therefore not recommended in the treatment of dysfunctional uterine bleeding. Uterine artery embolization is a new therapeutic approach for patients in whom surgery would be difficult to perform. The long-term efficacy and safety of this new surgical treatment modality have not yet been demonstrated.

Hysterectomy is the most widely used treatment. It can be performed abdominally, vaginally or laparoscopically. The vaginal and laparoscopic approaches are reported to cause fewer complications and to result in a shorter hospital stay and convalescence than the abdominal approach. Although hysterectomy guarantees the permanent cessation of menstrual flow and yields a high level of satisfaction, it is a major procedure. Its invasiveness, the morbidity, mortality and costs that it incurs, and the risk of late complications that it carries have led to the development of new treatments.

Endometrial ablation

Dysfunctional uterine bleeding is the main indication for endometrial ablation. Endometrial ablation seems to be the surgical treatment of choice for dysfunctional uterine bleeding and should be preferred to hysterectomy. It provides symptomatic relief without the need to remove most of the healthy uterus.

One of the drawbacks of endometrial ablation is the risk of persistent or recurrent bleeding, which requires a repeat ablation or possibly a hysterectomy. The reoperation rates given in published studies range from 0 to 38.2%, with the higher rates observed in longer studies or in women under the age of 35.

Pregnancy is rare but possible after endometrial ablation. Such pregnancy carries risks. It is also possible for endometrial cancer to develop in residual endometrium after an ablation, and such cancer can be difficult to diagnose because of the scar tissue that forms in the uterus. Lastly, the effects of hormone replacement therapy on residual endometrium in postmenopausal women are still unknown.

First-generation ablation techniques

The first-generation techniques are usually performed under general anesthesia but can also be performed with local or regional anesthesia. They require direct visual monitoring of the uterine cavity by means of a hysteroscope and an irrigation fluid. Even if the uterine cavity appears normal on hysteroscopy, an endometrial biopsy should be performed because hysteroscopy alone cannot rule out the possibility of a tumor or carcinoma of the endometrium. These techniques are sometimes grouped under the heading of hysteroscopic endometrial ablation techniques.

The complications associated with the first-generation ablation techniques include cervical laceration and uterine perforation. Bowel injury can occur as a result of the conduction of electrical current or direct trauma. The media used to distend the uterine cavity during hysteroscopy can cause fluid overload, allergic reactions and other systemic toxic reactions. Hemorrhage can occur if the ablation extends too deeply into the myometrium and large blood vessels are severed. Lastly, air embolism is a rare complication of operative hysteroscopy, but it can cause death.

The first-generation techniques offer considerable advantages over hysterectomy. They take less time to perform and require a much shorter hospital stay and convalescence. Although hysterectomy guarantees the cessation of menstrual flow and yields a higher level of satisfaction, it carries a greater risk of complications than endometrial ablation.

Transcervical resection

In accordance with the Agency's terminology and criteria, transcervical resection of the endometrium is considered an accepted technique. The results of a meta-analysis of six randomized controlled trials and of several other studies indicate that this technique is safe, with reproducible results. It is relatively effective in reducing the quantity of menstrual blood loss and yields a high level of satisfaction. Some of the advantages of transcervical resection of the endometrium include the possibility of performing an endometrial biopsy in order to rule out the presence of a tumor and the possibility of surgically removing intrauterine lesions. On the other hand, this technique requires a high level of surgical skill and carries a greater risk of uterine perforation and systemic absorption of irrigation fluid as a result of blood vessel exposure. However, transcervical resection of the endometrium causes few serious complications, especially if a rollerball electrode is used to treat the uterine fundus and cornual regions. Of the contraindications to transcervical resection of the endometrium, particular mention should be made of hemodynamic instability, coagulopathies and anticoagulant therapy.

Rollerball ablation

Rollerball endometrial ablation is an accepted technique as well. According to published studies, it compares with transcervical resection of the endometrium in terms of efficacy, the level of satisfaction and the reoperation rate. It is the easiest first-generation technique to master and the quickest to perform. Rollerball endometrial ablation causes fewer intraoperative complications than transcervical resection of the endometrium, carrying a lower risk of uterine perforation and fluid absorption, since the tip of the rollerball is blunt. Among other things, this technique is especially indicated for uterine bleeding secondary to anticoagulant therapy.

Laser ablation

According to published studies, laser endometrial ablation is comparable to transcervical resection of the endometrium in terms of efficacy, the level of satisfaction and the reoperation rate. The main drawbacks of laser endometrial ablation are the cost and length of the procedure. Furthermore, this technique requires more surgical skill, but it does offer the advantage of causing fewer intraoperative complications than transcervical resection of the endometrium. In Québec, laser endometrial ablation stopped being performed about ten years ago.

Second-generation ablation techniques

Most manufacturers attempt to market second-generation techniques by presenting them as procedures that can be performed on an outpatient basis. It is important that physicians and patients be aware of the diameter of the device to be introduced into the uterus. Given that these new techniques are performed without visual hysteroscopic monitoring (with the exception of hydrothermal endometrial ablation), the physician should make a diagnosis based on a visual examination prior to treatment, as well as a diagnosis supported by a pathophysiological study which includes a hysteroscopy and, at the very least, an endometrial biopsy. It is also advisable to perform a hysteroscopy after the treatment to check that only the uterine cavity was treated.

When this report was being drafted, five second-generation techniques had been the subject of rigorous assessments involving a comparison with established techniques. Only microwave endometrial ablation and impedance-controlled endometrial ablation had been compared with the standard conventional technique, transcervical resection of the endometrium. In the case of thermal balloon endometrial ablation, hydrothermal endometrial ablation and endometrial cryoablation, the comparator technique was rollerball endometrial ablation. Unfortunately, searches in the computerized literature databases did not yield any reports from randomized controlled trials of endometrial laser intrauterine thermotherapy. Given the paucity of published data, this technique was not included in our assessment and is only briefly described in appendix B.

Compared to the first-generation techniques, the second-generation techniques assessed in this report offer the advantage of being quick, easy and amenable to local anesthesia or narcosis, and they cause fewer intraoperative complications. However, they do carry a risk of complications, including hematometra, infection and internal organ injury. It would be useful to examine these techniques further to determine their cost-effectiveness and to confirm their safety when performed by a gynecologist who has not received special training (in the event that they are performed in clinics).

Thermal balloon ablation

Of the second-generation ablation techniques, only thermal balloon endometrial ablation is considered accepted. The long-term results of a randomized, controlled trial and those of several other studies indicate that this technique compares with transcervical resection of the endometrium in terms of efficacy and the reoperation rate. Very few studies have examined the level of satisfaction. Furthermore, this technique seems to be reserved for normal uterine cavities and causes pain because of uterine distention. Uterine retroversion appears to be associated with a greater risk of treatment failure. Among the contraindications to thermal balloon endometrial ablation, particular mention should be made of an active genital or urinary tract infection and any anatomic abnormality or any disease that can cause myometrial weakening. When this report was being drafted, the use of thermal balloon endometrial ablation was still not very widespread in Québec.

Microwave ablation

We have fewer data on microwave endometrial ablation than on the first-generation techniques or thermal balloon endometrial ablation. Based on the medium-term results of a randomized, controlled trial and those of a few uncontrolled trials, microwave endometrial ablation compares with transcervical resection of the endometrium in terms of efficacy, the level of satisfaction and the reoperation rate. However, as of yet, there are no published long-term results of large, randomized, controlled trials. Such results would enable one to better determine the impact of the therapeutic effects and, more specifically, the reoperation rate, which seems to plateau within three years after the initial procedure. This is why this technique is considered innovative. There is the potential for microwave endometrial ablation to be incomplete in women with an enlarged and highly deformed uterine cavity. It should be noted that the cervix has to be dilated to 9 mm in order to insert the waveguide and that the dilatation process can be painful, even with local anesthesia.

Hydrothermal ablation

Hydrothermal endometrial ablation is considered an innovative technique, too. We have few data on this technique, and, as of yet, there are no published long-term results of large, randomized, controlled trials. Published reports indicate that this technique and transcervical resection of the endometrium compare in terms of efficacy and the reoperation rate. Few studies have examined the level of satisfaction. The diagnostic hysteroscopy performed prior to treatment enables the physician to check that there are no uterine perforations and to detect any intrauterine pathology not previously diagnosed. Controlled irrigation of the uterine cavity with heated normal saline can reportedly be used to treat benign tumors that are sometimes present in the uterus. It is important to carefully select candidates for this operation, since a large fibroid deforming the uterine cavity would prevent adequate irrigation. Among the contraindications to hydrothermal endometrial ablation, particular mention should be made of an active genital or urinary tract infection and any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy. It should be noted that the cervix has to be dilated to 8 mm in order to insert the device and that the dilatation process can be painful, even with local anesthesia.

Cryoablation

Endometrial cryoablation is also considered an innovative technique. We have few data on this technique, and, as of yet, there are no published long-term results of large, randomized, controlled trials. Based on the results of one randomized, controlled trial, endometrial cryoablation compares with transcervical resection of the endometrium in terms of efficacy, the level of satisfaction and the reoperation rate. Hysterosonography is performed to check that the cryoprobe is properly positioned in the uterine cavity and to monitor the growth of the iceball during the treatment cycles. Uterine fibroids do not seem to affect the growth of the iceball and are easily destroyed by freezing. Endometrial cryoablation is especially contraindicated in the presence of an active genital or urinary tract infection and any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy.

Impedance-controlled ablation

Impedance-controlled endometrial ablation is considered an innovative technique as well. We have few data on this technique, and, as of yet, there are no published long-term results of large, randomized, controlled trials. Based on the results of one randomized, controlled trial, impedance-controlled endometrial ablation compares with transcervical resection of the endometrium in terms of efficacy, the level of satisfaction and the reoperation rate. Impedance-controlled ablation offers the advantage of not requiring preoperative endometrial thinning. This procedure can be performed at any time during the menstrual cycle, even during menstruation. Impedance-controlled endometrial ablation is contraindicated in the presence of an active genital or urinary tract infection and any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or previous transmural myomectomy. Furthermore, if the uterine cavity is less than 4 cm in length, the treatment will cause thermal injury to the endocervical canal. It should be noted that the cervix has to be dilated to 8 mm in order to insert the device and that the dilatation process can be painful, even with local anesthesia.

Endometrial laser intrauterine thermotherapy

Lastly, there are very few scientific publications on the second-generation technique that is not assessed in this report, namely, endometrial laser intrauterine thermotherapy. Consequently, there are few clinical data on its efficacy and safety. This is why this technique is considered experimental. Rigorous studies would need to be conducted to determine the efficacy, safety and cost-effectiveness of endometrial laser intrauterine thermotherapy and the associated level of satisfaction and long-term reintervention rate. It would also be useful to examine this technique further to confirm that it is safe when performed by a gynecologist who has not received special training (in the event that it is performed in clinics).

Economic repercussions of endometrial ablation in the treatment of dysfunctional uterine bleeding on Québec's health-care system

Endometrial ablation is a surgical procedure that is gaining in popularity, as evidenced by the fact that its frequency increased by nearly 82% between 1995 and 1999. In Québec, most endometrial ablations are performed in women aged 35 and older.

The decision to perform a hysterectomy can depend on how physicians diagnose and practice and on their experience and opinions of the efficacy of this procedure. In turn, these factors can depend on how recently the physician was trained and the availability of the new types of treatment and of equipment in Québec hospitals. Certain regional variations in the frequency of endometrial ablation observed in Québec may be due to whether or not the patients live in an urban setting, where the technical skill and the expertise have already been acquired.

The first-generation techniques entail lower costs than hysterectomy. The cost differential persists for a considerable period of time, although this gap narrows because of the relatively high reoperation rate in the years following endometrial ablation. Performing vaginal or laparoscopic hysterectomies could contribute to narrowing this difference.

Quantifying the economic repercussions of the second-generation techniques is no easy task. These techniques involve relatively high purchase and utilization costs (single-use devices). The five second-generation techniques assessed in this report seem comparable to the first-generation techniques already performed in Québec in terms of efficacy, the level of satisfaction and the reoperation rate. From an economic standpoint, the potential benefits of these new techniques include the fact that they take less time to perform and have a lower incidence of intraoperative complications. However, the clinical impact of these two benefits has not yet been demonstrated.

The amounts spent at Québec hospitals for endometrial ablation are not made public. For now, only the purchase cost of the different apparatuses and the expenses incurred for the single-use devices can be compared.

Conclusion

Medical treatment is seldom a lasting solution to dysfunctional uterine bleeding and is not without adverse effects. Although it is a type of definitive treatment, hysterectomy not only carries a considerable surgical risk, but also has certain drawbacks and is fairly expensive. In addition, it can cause many psychological and physical changes in women. However, hysterectomy continues to yield a high level of satisfaction, since it guarantees the cessation of bleeding.

Endometrial ablation has been proposed because it is a less invasive, more convenient and less expensive procedure when no other gynecologic condition is involved. Women with dysfunctional uterine bleeding prefer endometrial ablation to hysterectomy because this type of treatment enables them to avoid major surgery and because the hospital stay and convalescence are shorter.

Various energy sources have been used to destroy the endometrium, and all seem comparable in terms of efficacy and the reoperation rate. Since hysteroscopic endometrial ablation (by laser, rollerball or transcervical resection) and thermal balloon endometrial ablation have accepted status, there would be no particular conditions governing their use.

On the other hand, because they are innovative techniques, microwave endometrial ablation, hydrothermal endometrial ablation, endometrial cryoablation and impedance-controlled endometrial ablation should be reserved for certain hospitals with the necessary resources and knowledge for systematically gathering and for analyzing all the data arising from their use and for disseminating these data to the medical and scientific communities. Clinical trials with a follow-up of at least three years after the initial ablation should be conducted to demonstrate the efficacy of these techniques and to determine the long-term reoperation rate. It would be useful to investigate these techniques further to determine their cost-effectiveness and to confirm that they are safe when performed by a gynecologist who has not received special training (in the event that they are performed in clinics).

Lastly, because of its experimental nature, endometrial laser intrauterine thermotherapy (a second-generation technique not assessed in this report) should be the subject of rigorous studies aimed at demonstrating its immediate and long-term efficacy and safety and at determining its cost-effectiveness and the reoperation rate. Also, the use of this technique should be governed by the conditions that apply to innovative techniques.

Technologically, endometrial ablation is evolving at an extremely rapid pace, with large studies of the second-generation techniques presently underway or recently completed. The results of these clinical trials should be published within 12 to 24 months. These rapid changes require instituting a monitoring process and periodically publishing updates, which would enable one to reassess the specific status of each endometrial ablation technique.

In conclusion, we often observe a gap between clinical practice and evidence-based evaluative research. The incidence of surgical complications, the ease of use, and personal clinical experience clearly contribute to forming an opinion of the clinical utility and efficacy of any treatment. In addition, improvements to and the rapid diffusion of new techniques facilitate their adoption by clinicians, even in the absence of published scientific data.

Repercussions on the practice of medicine and on public health

Women's expectations and preferences seem to be important determining factors for the best type of surgical treatment for dysfunctional uterine bleeding. Often, a woman with dysfunctional uterine bleeding does not want a hysterectomy or even the cessation of menstrual flow but seeks above all relief from this bothersome symptom. If given the option, many will choose to keep their uterus. However, the new, much less invasive methods will not entirely supplant hysterectomy in the treatment of dysfunctional uterine bleeding. Some women will want menstruation to stop, and hysterectomy is currently the only type of surgical treatment for dysfunctional uterine bleeding that can guarantee this.

Since the second-generation endometrial ablation techniques require less surgical skill and experience, we should observe an increase in the number of gynecologists offering these therapeutic options and, consequently, greater access to these techniques by Québec women. Steps will necessarily have to be taken to ensure that surgeons have not only the technical skills, but also the training needed to carefully select candidates for this type of treatment. This is because a good knowledge of the indications and contraindications has a direct impact on the level of satisfaction with the treatment and on the failure and reoperation rates.

A woman with dysfunctional uterine bleeding who requests an endometrial ablation should have completed her family. A woman of child-bearing potential who is sexually active should subsequently use contraception, since she can become pregnant after the ablation. In postmenopausal women, the effects of hormone replacement therapy on residual endometrium are unknown. Any woman whose endometrium has been ablated and who is on hormone replacement therapy should receive an estrogen-progestin combination. Furthermore, it is possible for cancer to develop in residual endometrium after an ablation, and such cancer can be difficult to diagnose because of the scar tissue that forms in the uterine cavity. This is why one should evaluate the status of any woman with suspicious symptoms after an endometrial ablation.

The availability of the new techniques for treating dysfunctional uterine bleeding could lead women to seek surgery sooner than if hysterectomy were the only procedure available. Milder cases, which are normally treated by more conservative methods, could undergo less invasive treatment and experience an easier convalescence with endometrial ablation. Some women with serious medical conditions who would not tolerate general anesthesia and intra-abdominal surgery could have their problem, otherwise potentially life-threatening, taken care of with the new techniques.

The subsequent increase in the frequency of surgery should be offset by the decrease in the use of long-term drug therapy, although such therapy is not always effective and sometimes causes adverse effects. The new costs associated with endometrial ablation should therefore be weighed against potential drug savings. The changes that can affect the quality of life and productivity of patients who abandon medical treatment for endometrial ablation should be taken into account as well.

Unlike hysterectomy, endometrial ablation does not guarantee the cessation of menstrual flow and may require reoperation during the years following the initial procedure. The new endometrial ablation techniques involve relatively high equipment purchase and utilization costs. Furthermore, adopting a technique as minimally invasive as endometrial ablation could lead to substantial changes in the hospital infrastructure.

The patient's perspective on the cost of the new surgical procedures is very likely different. All the endometrial ablation techniques involve less post-operative pain and are characterized by a speedier recovery. Endometrial ablation could offer benefits for women's health, thanks to the lasting decrease in menstrual flow.

For all of these reasons, the repercussions of endometrial ablation techniques and, consequently, their role in the treatment of dysfunctional uterine bleeding can be fully defined only after a long-term follow-up.

GLOSSARY

Adenomyosis

The presence of endometrial tissue in the uterine muscle. It manifests as bleeding and pelvic pain. Called also *endometriosis interna* or *uterina*.

Amenorrhea

The absence of menses, outside of pregnancy, in a woman of menstrual age.

Anaphylactoid reactions

Anaphylactoid reactions are clinically similar to anaphylaxis but can occur after the first injection of certain drugs. They are associated with a dose-dependent idiosyncratic toxic mechanism rather than with an immunological mechanism.

Antifibrinolytic

An agent that inhibits the dissolution of blood clots. Used in the treatment of certain types of bleeding.

Classic cesarean section

A surgical incision made in the body of a pregnant uterus in order to remove the fetus and placenta. When performed at the end of pregnancy or during labour, the incision is almost always made in the lower segment of the uterus, but when a segment cesarean is impossible or contraindicated (before the lower segment has formed, in particular, in certain therapeutic abortion techniques), the incision is made in the body of the uterus.

Cornual region

One of the two upper angles of the inverted triangle formed by the uterine cavity and from which the fallopian tubes extend.

Cryoablation

An ablation technique using cold.

Cryoprobe

An instrument used in surgery to apply cold to deep tissues on a very localized basis.

Diathermal

Said of a surgical procedure aimed at destroying tissues by heat created when high-frequency alternating current flows between two electrodes.

Dysmenorrhea

Difficult and painful menstruation.

Electrocauterization

The destruction of tissue by means of an electrocautery, or wire loop, raised to a high temperature by electrical current.

Electrocoagulation
The destruction of tissue by coagulating the cytoplasm of its cells. It is caused by the heat emitted when high-frequency electrical current flows between a needle electrode (punctiform) and a large-surface electrode in contact with the patient.

Endometrial ablation
A surgical procedure consisting in removing the endometrium.

Endometriosis
The ectopic presence, outside the uterine mucous membrane, of functional endometrial tissue. Endometriosis can cause pelvic pain, which increases during menstruation, and reduced fertility. It can also lead to the formation, in the pelvic cavity, of cysts (endometriomas), which are sensitive to cyclical hormonal fluctuations and which can bleed during menses.

Endometritis
Inflammation of the uterine mucous membrane.

Endometrium
The inner mucous membrane of the uterus, whose structure varies with the levels of different hormones and whose desquamation, at the end of each menstrual cycle, results in menses.

Endosurgery
A deep, minimally invasive surgical technique performed in large-caliber blood vessels and internal organs by catheterization or fibroscopy.

Eumenorrhea
Menstruation that is normal in terms of duration and volume.

Fibroid
A uterine tumor consisting of connective tissue and smooth muscle tissue. Histologically, it is a myoma. Fibroids are also often called *uterine fibromyomas* or *leiomyomas*.

Gonadotropin-releasing hormone
A polypeptide synthesized in the hypothalamus. It is transported to the anterior lobe of the pituitary gland and stimulates the synthesis and release of both gonadotropins (sex hormones).

Hematometra
A mass resembling a tumor in appearance due to the retention of menstrual blood in the uterus as a result of cervical atresia or total vaginal aplasia.

Hemostasis
The arrest, whether spontaneous or therapeutic, of bleeding.

Hypomenorrhea
Very light menstrual flow.

Hysterosonography
An ultrasound technique for visualizing the uterus by means of an ultrasound transducer placed on the lower part of the abdomen over the uterus.

Impedance
The resistance offered by an anatomical structure ("electrical circuit") to the flow of an alternating current traveling through it.

Laparoscopy
A direct visual examination, for diagnostic or therapeutic purposes, of the abdominal cavity, distended beforehand by pneumoperitoneum, with the aid of an endoscope (laparoscope) inserted through the abdominal wall. Called also *celioscopy*.

Laparotomy
A surgical incision through the abdominal wall and peritoneum.

Leiomyoma
A benign tumor consisting of mature smooth muscle cells. Tumors of this type occur most often in the uterus (such tumors are improperly called *fibroids*).

Menorrhagia
Abnormally heavy and prolonged menstrual flow (menstruation usually lasts from three to five days).

Metrorrhagia
Uterine bleeding unrelated to menses that occurs between menstrual periods or after menopause.

Myomectomy
The removal of a uterine myoma (fibromyoma) with preservation of the uterus.

Myometritis
Inflammation of the myometrium.

Myometrium
The muscle coat of the uterus.

Narcosis
Reversible, artificial sleep produced by the administration of drugs (narcotic, general anesthesia).

Photocautery
Destruction of tissue by means of a laser beam.

Resectoscope
An endoscopic surgical instrument introduced into natural cavities and passages for the purpose of resecting tissues or organs.

Rhabdomyolysis
The more or less extensive destruction of striated muscle due to various causes, such as severe ischemia, myopathies, poisoning, mechanical crushing or intense muscular activity.

Stenosis
Permanent, pathologic narrowing of an orifice, a duct or a hollow organ. It can be congenital or acquired.

Transcervical resection of the endometrium
The complete or partial surgical removal of the inner mucous membrane of the uterus, starting at its fundus and proceeding toward its isthmus, by means of a sharp instrument introduced through the cervix.

Uterine retroversion
A deviation of the uterus in which its body, instead of tilted forward as it normally is, is tipped toward the back from its isthmus, the cervix thus pointing upward and forward.

LIST OF ABBREVIATIONS

CG	Control group
CI	Confidence interval
CO_2	Carbon dioxide
DVT	Deep venous thrombosis
EG	Experimental group
FDA	Food and Drug Administration (United States)
GHz	Gigahertz
GnRH	Gonadotropin-releasing hormone
HAD	Hospital Anxiety and Depression Scale
HPFB	Health Products and Food Branch (Canada)
HTA	Hydro ThermAblator®
HTAC	Health Technology Advisory Committee (United States)
IUD	Intrauterine device
kHz	Kilohertz
kPa	Kilopascal
MDA	Medical Devices Agency (United Kingdom)
MEA	Microwave Endometrial Ablation™
Nd:YAG	Neodymium: yttrium-aluminum-garnet laser
NHS	National Health Service (United Kingdom)
NHSCRD	NHS Centre for Reviews and Dissemination (United Kingdom)
NSAIDs	Nonsteroidal antiinflammatory drugs
OR	Odds ratio
QALY	Quality-adjusted life-year
®	Registered trademark
RAMQ	Régie de l'assurance maladie du Québec
RR	Relative risk
SD	Standard deviation
SF-36	Short Form 36
™	Trademark
WMD	Weighted mean difference

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1

INTRODUCTION

Dysfunctional uterine bleeding is one of the most common reasons for referral to a gynecologist. It is the main reason for consultation in more than 50% of women who undergo hysterectomy [NHSCRD, 1995]. The notion of dysfunctional uterine bleeding is a highly subjective one, and systematically measuring menstrual blood loss is not feasible in clinical practice. Often, there is no apparent condition or abnormality that can explain the bleeding. Nonetheless, some women consider their quality of life so diminished because of their menstruation that they wish to undergo medical or surgical treatment in order to eliminate (or at least alleviate) the problem. The main objective of treatment is to achieve symptomatic relief and improve the woman's quality of life.

The primary treatment of dysfunctional uterine bleeding is usually medical and involves the administration of hormones, nonsteroidal antiinflammatories (NSAIDs) and antifibrinolytics. However, when drug therapy fails, surgical treatment is often the next option. Hysterectomy has, for a long time, been the definitive treatment for dysfunctional uterine bleeding [Lethaby and Hickey, 2001]. It guarantees the cessation of menstrual blood loss, and most women are extremely satisfied after the operation. However, it is a major surgical procedure with inherent risks and the potential for complications. Most hysterectomies performed in Québec are performed abdominally, but the number and proportion of hysterectomies performed vaginally or laparoscopically is on the rise [Millar, 2001]. Vaginal and laparoscopic hysterectomies require a shorter hospital stay than abdominal hysterectomy [Kovac et al., 1991; NHSCRD, 1995]. Furthermore, the latest surgical procedures offer a shorter convalescence and lead to fewer complications than abdominal hysterectomy [Hidlebaugh, 2000; Lethaby et al., 2000d]. Many women prefer a less invasive surgical treatment, although the success of such a procedure is not always guaranteed [Lethaby and Hickey, 2001].

Goldrath et al. were the first to report the success of hysteroscopic endometrial ablation by laser photovaporization. This surgical procedure permits preservation of the uterus and reduces uterine bleeding in most patients [Goldrath et al., 1981]. The first-generation ablation techniques are performed hysteroscopically and are based on the use of laser or electrosurgical techniques. They are designed to destroy the entire thickness of the endometrium. Although very effective, these techniques carry certain risks. Furthermore, they are often complex to perform and require an experienced surgeon.

A second generation of endometrial ablation techniques is therefore being developed. These new procedures are technically simpler and carry fewer risks. Microwave endometrial ablation, which is currently under investigation, is one of these techniques.

In the fall of 2000, the ministère de la Santé et des Services sociaux du Québec submitted an assessment request to the Agence d'évaluation des technologies et des modes d'intervention en santé, asking it to define the role of microwave endometrial ablation in the treatment of dysfunctional uterine bleeding.

In response to this request, the Agency commissioned the drafting of this assessment report, which mainly examines the efficacy, safety and acceptability of microwave endometrial ablation. The report compares this technique with transcervical resection of the endometrium, the procedure currently performed in Québec hospitals for dysfunctional uterine bleeding.

However, a decision was made to broaden the scope of this report in order to document the situation in Québec regarding the practice of endometrial ablation in the surgical treatment of dysfunctional uterine bleeding. Consequently, the report also determines the specific status of each technique in accordance with the classification developed by the Agency

[CETS, 1998]: experimental, innovative and accepted status (see Appendix A). Secondly, we examined the health-care costs associated with the surgical treatment of dysfunctional uterine bleeding.

2

RESEARCH METHODOLOGY

We performed a literature search for the purpose of evaluating the efficacy and safety of the various endometrial ablation techniques and, specifically, the advantages of microwave ablation in the treatment of dysfunctional uterine bleeding, in order to shed better light on the usefulness of this technique.

Systematic searches were performed in computerized literature databases for the period from 1981 to 2002. We chose to search back to 1981 because this was approximately when considering endometrial ablation in the treatment of dysfunctional uterine bleeding began. The cut-off date for the list of published studies examined was July 31, 2002.

The computerized literature databases consulted were as follows:

- MEDLINE
- Current Contents
- Cochrane Collaboration
- NHS Centre for Reviews and Dissemination (NHSCRD)
- FDA Center for Devices and Radiological Health

The search was based on the following keywords: dysfunctional uterine bleeding, menorrhagia, menometrorrhagia, metrorrhagia, excessive menstrual blood loss, heavy menstrual bleeding, endometrial ablation, hysteroscopic, global, microwave, rollerball, transcervical resection of the endometrium, laser ablation, thermal balloon, hydrothermal ablation, cryoablation, cryosurgery, endometrial laser intrauterine thermotherapy and medical therapy.

An exhaustive description of endometrial ablation techniques and of the potential complications is beyond the scope of this report. Given the availability of research reports, we only assessed the endometrial ablation techniques that had been examined in rigorous studies (including at least one randomized, controlled trial) of their efficacy and safety. A detailed description of these techniques is provided in Appendix B. Since there are very few clinical data on the techniques that are still in the experimental stage, we only describe these techniques briefly in the appendix. Endometrial ablation techniques (or devices) that had been abandoned when this report was written were excluded.

We used the lists of references at the end of clinical trial papers that had already been examined, in order to conduct a systematic search. When necessary, we contacted the authors in order to obtain a reprint of a published or unpublished scientific article. Lastly, we consulted experts in gynecology.

2.1 Efficacy criteria

The occurrence of amenorrhea (complete absence of menstrual blood loss) is often used as a criterion for evaluating the treatment outcomes of endometrial ablation. Despite the fact that amenorrhea is often the main efficacy criterion used in clinical studies, hypomenorrhea (a quantitative decrease in menstrual blood loss), is the usual treatment outcome. Total hysterectomy is the only surgical treatment for dysfunctional uterine bleeding that guarantees amenorrhea [Garry, 1995b; Grant et al., 1999; HTAC, 2000; Ke, 1997; Meyer et al., 1998].

Prospectively documenting menstrual blood loss using a validated pictorial chart method [Higham et al., 1990; Janssen et al., 1995] is now an integral feature of recent clinical trials concerning the treatment of dysfunctional uterine bleeding [Corson, 2001; FDA, 1997; FDA, 2001b; FDA, 2001d; FDA, 2001f; Heppard et al., 2001; Meyer et al., 1998]. Briefly, the participants are asked to record the extent of their menstrual blood loss each day by marking on a diagram the size of the blood spots on their items of sanitary protection (including tampons) and the number of such items used. The entries are then converted to diary scores. A diary score of 100 offers 86% sensitivity and 81% specificity with regard to the actual loss of at least 80 mL of menstrual blood and is indicative of clinical menorrhagia [Higham et al., 1990]. Any woman with a score of 150 is therefore menorrhagic (inclusion criterion). Therapeutic success is based on a reduction in baseline scores greater than or equal to 150 to 75 or less one year after the initial intervention. Using such evaluution methods improves study population homogeneity and permits interstudy comparisons.

However, a 50% reduction in menstrual flow may be satisfactory for one woman but not for another. This is why the subjective evaluation of treatment outcomes by a treated woman (satisfaction, quality of life) was used as a secondary efficacy criterion and could be a more important indicator of therapeutic success than the induction of amenorrhea [Amso et al., 1998; Garry et al., 1995; HTAC, 2000; Weber, 2002].

3

DYSFUNCTIONAL UTERINE BLEEDING

3.1 Definition

Dysfunctional uterine bleeding refers to a symptomatology that includes any uterine bleeding in the absence of pregnancy, neoplasm, infection or other organic abnormalities or conditions [Swartz and Butler, 1992].

There are two types of uterine bleeding, menorrhagia and metrorrhagia. Menorrhagia is defined as abnormally heavy and regular menstrual blood loss. Clinically, menorrhagia is blood loss of at least 80 mL per period [HTAC, 2000; Kammerer-Doak and Rogers, 2000; Lethaby et al., 2000d; NHSCRD, 1995; Prentice, 1999]. Metrorrhagia, on the other hand, is irregular uterine bleeding between two consecutive periods [Speroff et al., 1999].

Although systematically quantitating menstrual blood loss is possible, doing so is reserved for research and currently seems unfeasible in clinical practice [NHSCRD, 1995]. With no objective evaluation of menstrual blood loss, the notion of dysfunctional uterine bleeding is highly subjective. The factors that influence a given patient's perception of bleeding include her age, sociocultural background, physical activity level, personal hygiene, symptoms and psychological state [HTAC, 2000; Hurskainen et al., 2001; Ke, 1997]. Other factors can lead a woman to seek treatment, such as the effects of uterine bleeding on her sexual and psychological functioning, her work performance and her knowledge of treatments for dysfunctional uterine bleeding [HTAC, 2000; Ke, 1997].

3.2 Epidemiology

Dysfunctional uterine bleeding is frequent in women of reproductive age. In fact, its prevalence is especially high during adolescence and the decade preceding menopause [Speroff et al., 1999].

In an international study conducted by the World Health Organization, it was found that 1,011 of the 5,322 women (19%) surveyed from 14 different countries were menorrhagic [Snowden and Christian, 1983]. This rate is consistent with the results of a previous survey that had reported a worldwide prevalence of 20% [Hullberg et al., 1966].

In Canada, 48,572 women aged 35 and over had a hysterectomy in 1996-1997. The hysterectomy rate during that period was therefore 628 per 100,000 women in that age group. Dysfunctional uterine bleeding and dysmenorrhea (menstrual pain) were the main indication for 16.1% of the hysterectomies performed in Canada and the second leading reason for undergoing the procedure [Millar, 2001].

In the United Kingdom, more than 5% of women between the ages of 30 and 49 consult their general practitioner because of menorrhagia [Coulter et al., 1995; Grant et al., 2000; Lethaby et al., 2000d]. It accounts for 12% of referrals to a gynecologist and, after a consultation with the latter, surgical intervention is highly likely [Lethaby et al., 2000d; NHSCRD, 1995]. Grant et al. observed a direct relationship between referral to a gynecologist and hysterectomy [Grant et al., 2000]. No argument in favour of the hypothesis that an effective medical treatment prescribed by a primary care physician can lead to a decrease in the referral rate to a gynecologist and in the hysterectomy rate was found [Grant et al., 2000; NHSCRD, 1995].

3.3 Pathophysiology

The most frequent cause of dysfunctional uterine bleeding is anovulation. If it is not exposed to progesterone and does not shed periodically, the endometrium will attain an abnormal height without concomitant structural support. In fact, unopposed estrogen therapy causes the formation of endometrial tissue containing relatively little stroma and back-to-back glandularity. The spontaneous and repeated breakage of this fragile endometrium results in uterine bleeding [Speroff et al., 1999; Swartz and Butler, 1992]. In the absence of the normal control mechanisms that limit menstrual blood loss, such uterine bleeding can be prolonged and excessive. If unopposed by the administration of a progestin, estrogenic stimulation can, over time, cause a hyperplastic response in the proliferating endometrium [Swartz and Butler, 1992].

According to an alternative hypothesis, the nonhormone-related regeneration of the surface epithelium from basal glands and cornual area residual tissue, together with restoration of the binding tissue, is critical in the cessation of menstrual flow. Therefore, uterine bleeding secondary to unopposed estrogen therapy is uncontrolled because there is insufficient stimulus (loss of tissue) to trigger binding surface restoration [Speroff et al., 1999]. Further studies will need to be conducted to reconcile the differences of opinion concerning the pathophysiological processes involved in dysfunctional uterine bleeding.

Heavier uterine bleeding is associated with persistently high estrogen levels, which are observed, for example, in the presence of polycystic ovaries (Stein-Leventhal syndrome), obesity, immaturity of the hypothalamic-pituitary-gonadal axis (in perimenarchal adolescents) and late anovulation (usually in premenopausal women). Certain systemic diseases, such as diabetes, acute systemic lupus erythematosus, Cushing's disease, hyperthyroidism, hypothyroidism and hyperprolactinemia, can cause uterine bleeding, albeit rarely [HTAC, 2000; Ke, 1997; NHSCRD, 1995; Swartz and Butler, 1992]. Heavy and irregular uterine bleeding is often associated with a serious organ disease, such as renal or hepatic failure [Speroff et al., 1999].

The exact proportion of dysfunctional uterine bleeding occurring in the presence of ovulation has not been determined, but it is low. Laboratory studies have shown that fibrinolytic activity and prostaglandin production can increase in the endometrium of women who have this problem [Prentice, 1999]. When uterine bleeding occurs in the presence of ovulatory cycles, a more thorough investigation should be conducted to rule out hemorrhagic diathesis or some other condition [Swartz and Butler, 1992].

Up to 20% of adolescents with uterine bleeding have a coagulopathy, such as von Willebrand-Jürgens syndrome, chronic idiopathic thrombocytopenia, or leukemia. Uterine bleeding secondary to a blood dyscrasia, that is, a disorder affecting the development of blood components, is usually heavy, cyclical and regular. This same characteristic bleeding may be observed in women on anticoagulant therapy [Speroff et al., 1999; Swartz and Butler, 1992].

All gynecological cancers can cause dysfunctional uterine bleeding. Even common epithelial tumors of the ovary can produce estrogens and cause uterine bleeding. Submucous uterine leiomyomas and endometrial polyps may be present in older women [Swartz and Butler, 1992]. Bleeding can also result from a uterine infection [HTAC, 2000; Ke, 1997; NHSCRD, 1995].

Certain complications of pregnancy, such as spontaneous or incomplete abortion, fetal retention, subinvolution of the placental site (hypertrophy persisting after delivery) and placental polyps are very common causes of uterine bleeding. Uterine bleeding is frequent in the presence of trophoblastic disease and extrauterine pregnancy, but these conditions are rare [Speroff et al., 1999; Swartz and Butler, 1992]. Uterine bleeding is often associated with the various methods of contraception, especially the intrauterine device (IUD), and with hormone replacement therapy in postmenopausal women [HTAC, 2000; Ke, 1997; NHSCRD, 1995; Speroff et al., 1999]. Without realizing it, women can take medications that have different effects on the endometrium. Lastly, uterine bleeding can be idiopathic.

3.4 Diagnosis

Blood loss can be considered dysfunctional uterine bleeding if the woman reports the presence of blood clots, profuse or socially embarrassing bleeding, the need to wear one or two sanitary napkins (super or maxi) and to change them every half-hour, hour or every other hour, or a combination of these symptoms. Although the clinical history is usually used as a basis for evaluating uterine bleeding, irregular or prolonged bleeding is often recorded on a calendar. Blood loss can also be evaluated by the alkaline hematin test, in which hemoglobin extracted from sanitary napkins is measured [HTAC, 2000; Ke, 1997].

Iron-deficiency anemia is one of the consequences of excessive menstrual bleeding. In the West, dysfunctional uterine bleeding is the leading cause of iron deficiency anemia, and the alkaline hematin test is an objective method for measuring excessive menstrual bleeding [Prentice, 1999]. A laboratory diagnosis of iron deficiency anemia is the only available clinical test for detecting excessive bleeding [HTAC, 2000; Ke, 1997].

To a certain extent, dysfunctional uterine bleeding is diagnosed by a process of elimination. It is therefore essential to look for the cause of the bleeding. The investigation includes a physical and pelvic examination, and a history in which the patient is asked about her general health, medication use, contraception, bleeding patterns and cycle length. Blood tests are performed to determine cell counts and to rule out pregnancy. Paraclinical examinations that might be performed include screening cytology, an endometrial biopsy, dilatation and curettage, a pelvic ultrasound, a diagnostic hysteroscopy, and hysterosonography with normal saline irrigation. The treatment is selected after the cause or causes of the bleeding are determined. Treating any underlying condition or lesion may be sufficient to control excessive bleeding [Garry, 1995b; HTAC, 2000; Prentice, 1999; Vilos et al., 2001].

4

THE TREATMENT OF DYSFUNCTIONAL UTERINE BLEEDING

A thorough investigation should be conducted to rule out any organic disease before treating dysfunctional uterine bleeding. The objective of treatment is twofold: to eliminate excessive bleeding (by reducing or completely eliminating menstrual blood loss) and to improve the patient's quality of life [NHSCRD, 1995]. Dysfunctional uterine bleeding should be considered an endocrine disorder that is best treated first medically, the more invasive forms of treatment being reserved for refractory cases [Swartz and Butler, 1992].

4.1 Medical treatment

Candidates for drug therapy include women with no organic lesions, women whose uterine bleeding interferes with normal activities or causes anemia, those who wish to avoid surgery and those who wish to maintain their fertility [HTAC, 2000; Prentice, 1999].

4.1.1 Hormone therapy

Medical treatment involving the administration of progestins is the basis of therapy, since, in most cases of dysfunctional uterine bleeding, the underlying cause is anovulation, in which estrogen stimulation of the endometrium occurs without sufficient opposing progesterone. For many years, progestins were administered during the luteal phase of the menstrual cycle [Lethaby et al., 2000c; Prentice, 1999; Speroff et al., 1999]. We now know that this approach is ineffective, for progestins are effective when administered for 21 days during each menstrual cycle. Withholding treatment during the 7 remaining days of the cycle leads to withdrawal bleeding [Lethaby et al., 2000c; Prentice, 1999].

If the patient wishes to use contraception, it would be best that she takes oral contraceptives. The administration of depot-medroxyprogesterone acetate at the contraceptive dose is a useful option for women who are poorly compliant with oral treatment [Speroff et al., 1999]. The endometrium can be exposed directly to progestin with an IUD that releases progesterone or levonorgestrel.

The latest levonorgestrel IUD (Mirena™) is a T-shaped device with a steroid reservoir around the vertical stem that releases a steady amount of levonorgestrel (20 mg/24 hrs) [Prentice, 1999; Vilos et al., 2001; Working Party for Guidelines for the Management of Heavy Menstrual Bleeding, 1999]. The levonorgestrel IUD is more effective than progestins in the treatment of dysfunctional uterine bleeding. Women who use this IUD are more satisfied and more inclined to continue the treatment but experience more adverse effects, such as intermenstrual blood loss and breast tenderness [Lethaby et al., 2000b]. The levonorgestrel IUD could prove to be effective as a method of contraception and in the long-term treatment of dysfunctional uterine bleeding, and it could be an alternative to surgery for such bleeding. Study results indicated that between 64 and 80% of women on a waiting list for a hysterectomy cancelled the operation within six months following the insertion of the levonorgestrel IUD [Luukkainen, 2000; Prentice, 1999]. In Canada, when this report was being drafted, the levonorgestrel IUD was indicated solely for contraceptive purposes. It can also be used in the treatment of dysfunctional uterine bleeding if concomitant contraception is required [Lethaby et al., 2000b].

In young women with anovulatory cycles, dysfunctional uterine bleeding may be associated with prolonged endometrial buildup, delayed diagnosis and very heavy menstrual blood loss. In such cases, combined estrogen-progestin therapy is administered in the form of combined oral contraceptives. Any low-dose monophasic tablets are useful [Speroff et al., 1999]. However, after conducting a systematic review, Iyer et al. concluded that there were not enough quality data on this and that the results of the one clinical study identified were inadequate to assess the efficacy of estrogen-progestin contraceptives in the treatment of dysfunctional uterine bleeding [Iyer et al., 2000].

Light, intermittent vaginal bleeding is frequently associated with weak estrogen stimulation. When there is minimal endometrial tissue, progestin therapy has no beneficial effect because there is insufficient tissue on which the progestin could exert its effect. The same situation can be observed in younger women with anovulatory cycles in whom prolonged hemorrhagic desquamation leaves little residual tissue. In such cases, the physician can prescribe oral estrogens for 7 to 10 days. All cyclic estrogen therapy should be followed by the administration of a progestin and withdrawal bleeding [Speroff et al., 1999].

Danazol and gonadotropin-releasing hormone (GnRH) analogs are two options used in the treatment of menstrual bleeding refractory to the other forms of therapy [HTAC, 2000; Swartz and Butler, 1992]. Danazol effectively reduces uterine bleeding, but it has to be administered continuously at considerably high doses for a long period of time. The cost and androgenic adverse effects of danazol limit the usefulness of this therapeutic option and make it a second line of defense [Speroff et al., 1999]. GnRH analogs are also effective in reducing menstrual blood loss. However, certain adverse effects, such as hot flashes and a decrease in bone density, limit their use [Vilos et al., 2001].

4.1.2 Nonhormonal therapy

In the absence of disease, nonhormonal therapy should be considered the first approach to treatment in women with ovulatory cycles and uterine bleeding [HTAC, 2000; NHS, 1995; Prentice, 1999; Speroff et al., 1999]. Nonhormonal treatments offer the advantage of being administered only during menstruation and of being especially useful in women who do not require contraception or who do not wish to receive hormone therapy [Prentice, 1999].

Prostaglandins have important effects on the endometrial vasculature and, presumably, on endometrial hemostasis. These cyclooxygenase inhibitors reduce menstrual flow in women who ovulate normally [Speroff et al., 1999]. The efficacy of NSAIDs in the treatment of dysfunctional uterine bleeding was reported in a systematic review [Lethaby et al., 2000a]. Flufenamic and mefenamic acids are two NSAIDs that inhibit the cyclooxygenase enzyme required for the production of prostaglandins by the estrogen-stimulated endometrium. They are the NSAIDs of choice [HTAC, 2000; NHS, 1995; Prentice, 1999; Swartz and Butler, 1992]. When used in a limited fashion, they seldom cause adverse effects, since administration usually starts with the onset of menses and continues for three or four days [Speroff et al., 1999].

Since the levels of plasminogen activators (a group of enzymes that catalyze fibrinolysis) have been found to be higher in the endometrium of women with dysfunctional uterine bleeding than in those with normal bleeding, the use of fibrinolytic enzyme inhibitors (antifibrinolytics) has been promoted in the treatment of heavy menstrual bleeding [Cooke et al., 2000]. A systematic review reports the efficacy of antifibrinolytic treatment for dysfunctional uterine bleeding [Cooke et al, 2000]. Tranexamic acid is the antifibrinolytic of choice, despite the fact that it has not been routinely prescribed, this because of the risk of adverse effects with this type of drug, especially the increased risk of deep venous thrombosis (DVT). Long-term studies in Sweden, however, have shown that the incidence of thrombosis in women treated with tranexamic acid is comparable to the spontaneous frequency of thrombosis in women in general [Cooke et al., 2000].

4.2 Surgical treatment

Surgery is considered when the woman does not respond or becomes refractory to medical treatment or when such treatment is contraindicated or causes intolerable adverse effects [HTAC, 2000]. The following four procedures can be performed: curettage, total or subtotal hysterectomy (removal of the uterus with or without preservation of the cervix), uterine artery embolization and endometrial ablation (removal of the uterine mucous membrane) [HTAC, 2000; Kelleher and Braude, 1999; NHSCRD, 1995].

4.2.1 Curettage

Uterine curettage (performed after dilatation of the cervix) is a surgical procedure consisting in removing, by scraping with a curette, some of the uterine mucous membrane. The contents of the uterus are then aspirated. This procedure stabilizes uterine bleeding in some women. However, its effects are hardly ever long-lasting [HTAC, 2000; Working Party for Guidelines for the Management of Heavy Menstrual Bleeding, 1999].

For a long time, curettage was presented as one of the options for treating dysfunctional uterine bleeding. However, the efficacy of this procedure for this condition has never been demonstrated, and there are no published randomized, controlled trials on this topic [NHSCRD, 1995; Vilos et al., 2001]. Uterine curettage is not an effective treatment for dysfunctional uterine bleeding [Vilos et al., 2001]. It is therefore not recommended for this condition [Working Party for Guidelines for the Management of Heavy Menstrual Bleeding, 1999].

4.2.2 Hysterectomy

Hysterectomy is the most widely used treatment. It can be performed abdominally or vaginally. In addition, laparoscopic hysterectomy was recently developed [Lethaby et al., 2000d; NHSCRD, 1995]. There are considerable differences between these surgical procedures in terms of convalescence and costs [Lethaby et al., 2000d]. Hysterectomy can include the removal of one or both ovaries (total hysterectomy plus salpingo-oophorectomy). One can also perform only a myomectomy (surgical removal of a myoma) and preserve the integrity of the uterus [NHSCRD, 1995].

Although hysterectomy guarantees the cessation of menstrual blood loss and yields a high level of satisfaction, it is a major procedure [Lethaby and Hickey, 2001]. Thus, in their prospective, multicentre study, Dicker et al. found the morbidity rate due to abdominal and vaginal hysterectomy to be 42.8% and 24.5%, respectively [Dicker et al., 1982]. In addition, the incidence of mortality associated with abdominal hysterectomy performed for benign, nonobstetrical disease was approximately 10 cases per 10,000 operations. A recent retrospective, single-centre survey revealed comparable morbidity rates of 44.0% and 27.3% for abdominal and vaginal hysterectomy, respectively [Varol et al., 2001], and a mortality rate of 15 cases per 10,000 operations after hysterectomy performed for benign, nonobstetrical disease. It should, however, be noted that these high morbidity rates included infections and episodes of benign fever, which were the most common complications. Most likely, complex morbidity due to hysterectomy is much lower. Thus, the morbidity rate found upon a meta-analysis of the complications of laparoscopic hysterectomy was 15.6% [Garry and Phillips, 1995]. The vaginal and laparoscopic approaches cause fewer complications and result in a shorter hospital stay and convalescence than the abdominal approach [Hidlebaugh, 2000; Kovac et al., 1991; Lethaby et al., 2000d; NHSCRD, 1995]. However, vaginal or laparoscopic hysterectomy is contraindicated in some women.

The invasive nature of hysterectomy, the morbidity, mortality and costs that it incurs, and the risk of further complications, including adhesions, bowel and/or bladder injury, fever and infections, postoperative bleeding, and wound dehiscence, have led to the development of alternative treatments for dysfunctional uterine bleeding [Erian, 1994; Garry, 1995b; HTAC, 2000; Ke, 1997; NHSCRD, 1995].

4.2.3 Uterine artery embolization

Uterine artery embolization is an interventional, fluoroscopy-assisted vascular endosurgical technique. It consists in obstructing the vessels that supply blood to the uterus with synthetic microparticles for the purpose of treating hemorrhagic disorders or uterine fibroids, by catheterizing a femoral artery [Kelleher and Braude, 1999; Machan and Martin, 2001].

One of the main advantages of uterine artery embolization is that it can be used to treat fibroids that would otherwise warrant a hysterectomy, with preservation of the uterus. In addition, it constitutes a new therapeutic approach for patients in whom surgery would be difficult. The operation is performed with local or regional anesthesia and sedation, and requires a short hospital stay [Floridon et al., 2001; Kelleher and Braude, 1999; Machan and Martin, 2001]. The long-term efficacy and safety of this new surgical treatment are unknown, but researchers have reported postoperative infections causing significant morbidity and being potentially fatal [Floridon et al., 2001; Kelleher and Braude, 1999; Machan and Martin, 2001]. Therefore, until other results of large, randomized trials are published, this endosurgical technique should be considered a new approach that is still under investigation.

4.2.4 Endometrial ablation

Endometrial ablation was adopted in clinical practice toward the end of the 1980s as a less invasive alternative to hysterectomy for dysfunctional uterine bleeding. The first-generation ablation techniques are based on photocautery, electrocautery or electrocoagulation and are designed to destroy the entire thickness of the endometrium. All of these techniques require direct visual hysteroscopic monitoring of the uterine cavity irrigated with a solution. The monitoring also serves to detect and treat other intrauterine diseases, such as submucous fibroids and polyps.

Although the first-generation endometrial ablation techniques are clearly safe and effective, too little use is still made of them in certain cases, largely because of insufficient specialized training and the fear of surgical complications, such as uterine perforation and excessive fluid absorption [Cooper and Erickson, 2000]. This explains the efforts to develop most of the new endometrial ablation techniques. These second-generation techniques are designed to destroy the entire thickness of the endometrium while at the same time preventing the associated risks and obviating the skill requirements that the first-generation techniques entail. In fact, most of these new surgical techniques do not require surgical hysteroscopy (see Table 1).

A search in the computerized literature databases yielded a few recently published scientific articles on the efficacy and safety of the Vesta™ System (intrauterine electroballoon endometrial ablation) [Corson et al., 1999; Corson et al., 2000; Dequesne et al., 1997; Gallinat, 2000; Gallinat and Cosgriff, 2001]. In two of these articles, the authors

Table 1

Endometrial ablation techniques

Technique *Device*	With hysteroscopic monitoring	Pretreatment with endometrial thinning agents	Applicator diameter (mm)	Duration of treatment (min)	Approved in Canada
First-generation					
Laser ablation	Yes	Recommended		20 to 35	Yes
Transcervical resection	Yes	Recommended		15 to 20	Yes
Rollerball ablation	Yes	Recommended		15 to 30	Yes
Second-generation					
Microwave ablation					
Microwave Endometrial Ablation™	No	Recommended	8.0	1 to 7	Yes
Thermal balloon ablation					
ThermaChoice™ II[a]	No	Recommended	4.5	8	Yes
Cavaterm™ plus[b]	No	Recommended	6.0	10	Yes
MenoTreat™	No	Recommended	7.0	11	No
Hydrothermal ablation					
Hydro ThermAblator®	Yes	Recommended	7.8	10	Yes
EnAbl™	No	Recommended	5.0	15	No
Cryoablation					
Her Option™[c]	No[d]	Recommended	5.5	4 to 22	Yes
Soprano™	No	Recommended	5	5 to 8	No
Impedance-controlled ablation					
NovaSure™	No	Not necessary	7.0	0.67[e] to 2	Yes
Endometrial laser intrauterine thermotherapy					
GyneLase™[f]	No	Recommended	6	7	Yes

[a] Second-generation balloon.

[b] Second-generation catheter (the first catheter had a diameter of 8 mm, and the procedure took 15 minutes).

[c] Formerly First Option™.

[d] Ultrasound-guided.

[e] 0.67 minutes = 40 seconds.

[f] Technique also known under the trade name of Elit™ (Endometrial Laser Intrauterine Thermal Therapy™).

also provide the results of the medium-term and final analyses of a randomized, controlled trial of this device [Corson et al., 1999; Corson et al., 2000]. Curiously, the manufacturer stopped producing and marketing the Vesta in 1998[1]. Furthermore, it withdrew the request for approval previously filed with the U.S. Food and Drug Administration (FDA). When this report was being drafted, Valleylab was still the sole owner of this technology. Consequently, endometrial ablation techniques by radiofrequency emission or by means of the Vesta are excluded from this report.

Regardless of the technique used, the objective of endometrial ablation is to achieve amenorrhea or hypomenorrhea. However, the endometrium has a tremendous capacity to regenerate. It is therefore essential to destroy both the entire thickness of this mucous membrane and the superficial myometrium to effectively control menstrual blood loss. The tissue should be destroyed to a depth of at least 5 mm, since it is considered that endometrial glandular elements will almost invariably be present more deeply in the myometrium. The ablation should therefore be performed to a depth of 2.5 to 3.0 mm in the myometrium to prevent isolated regeneration of endometrium [Erian, 1994; Kammerer-Doak and Rogers, 2000; Lethaby et al., 2000d].

Ablation is more effective when the endometrium is 3 to 4 mm thick. To optimize the outcome, the procedure is usually performed at the end of the woman's period, during the proliferative phase of her menstrual cycle, or after endometrial curettage. As well, GnRH analogs can be used before the operation to achieve endometrial thinning or atrophy [Garry, 1995b; HTAC, 2000; Ke, 1997; Sowter et al., 2000]. The GnRH analogs whose use has been examined most often include goserelin acetate (a gonadotropin) and leuprolide acetate. Danazol is used for this purpose as well [Kammerer-Doak and Rogers, 2000; Sowter et al., 2000]. Adequate preparation of the endometrium reduces surgical time and improves operative results and safety [Garry, 1995b; HTAC, 2000; Sowter et al., 2000].

4.2.4.1 Selection criteria

The main selection criteria for endometrial ablation include:

- no organic lesions, such as cancer or precancerous lesions, of the endometrium or cervix and no lesions of the uterus or any underlying lesions requiring other types of surgery;
- no acute genital tract infection (cervicitis, endometritis or salpingitis);
- menorrhagia or abnormally heavy menstrual blood loss (> 80 mL per cycle), blood loss sufficient to cause anemia, or blood loss or symptoms that interfere with normal activities;
- drug treatment failed, was contraindicated or was refused, or the adverse effects were intolerable;
- uterine size less than that observed at 12 weeks' gestation; uterine cavity length less than 12 cm;
- no fibroids greater than 5 cm in diameter;
- must not have an absolute desire for amenorrhea (since it cannot be guaranteed);
- childbearing completed [Garry, 1995b; HTAC, 2000; Kammerer-Doak and Rogers, 2000; Ke, 1997; Parkin, 1998].

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[1] Telephone communication with T. Hilkemeier, Vice-president of Marketing, Valleylab, USA, April 2001.

4.2.4.2 Prognosis

Davis et al. observed that treatment failure (menstrual flow unchanged or heavier) was associated with the following three situations: the persistence of dysfunctional bleeding (due to the presence of residual endometrium, endometrial regeneration, endometriosis or adenomyosis); scarring complications (especially cervical stenosis); and the presence of uterine lesions when the ablation was performed (e.g., fibroids or adenomyosis) [Davis et al., 1998]. They did a histopathologic study of the uteri removed after rollerball endometrial ablation failure in order to detect any foci of endometrial tissue in the uterine cavity of those women who were still complaining of excessive bleeding. They also detected fibroids and adenomyosis in 30% and 27%, respectively, of the uteri thus removed. This type of study does not indicate which "diseases" might be detected in women after a successful endometrial ablation [Davis et al., 1998; Parkin, 1998; Parkin, 2000a].

In one randomized, controlled trial, the participants who had been clinically diagnosed with dysfunctional uterine bleeding underwent hysterectomy, laser endometrial ablation or transcervical resection of the endometrium [Pinion et al., 1994]. In the women treated by hysterectomy, the incidence of fibroids, endometriosis and adenomyosis was 20%, 8% and 17%, respectively. It is reasonable to expect a similar distribution of these conditions in the other two groups, but the incidence of hysterectomy secondary to laser ablation or transcervical resection was only 22%, even during the 4 - to 6 - year period following the first intervention. It can therefore be concluded that many women treated by endometrial ablation will be satisfied with the result of the procedure and will thus avoid hysterectomy, even if they have one of the above-mentioned conditions. Since they were detected upon hysterectomy after ablation failure, their importance could very well be overestimated, a situation that highlights the usefulness of randomized, controlled trials [Parkin, 1998; Parkin 2000a; Pinion et al., 1994].

Large, randomized, controlled trials and large prospective surveys have revealed certain prognostic factors. The main factor, true excessive menstrual blood loss, is associated with a better treatment outcome than more normal loss [Parkin, 2000a]. Thus, in one study, the investigators reported a subjective failure rate of 9% in the women with a menstrual blood loss greater than 80 mL and of 18% in those who considered their periods heavy but whose menstrual loss was normal [Gannon et al., 1996].

The patient's age also seems to play an important role. The probability of therapeutic success increases with age [Amso et al., 1998; Bongers et al., 2002; Boujida et al., 2002; Erian, 1994; Weber, 2002]. In addition, the level of satisfaction is lower in younger women than older women [Parkin, 1998; Parkin, 2000a]. Thus, an audit conducted in Scotland on hysteroscopic interventions revealed a 1-year posttreatment satisfaction rate of 79% and 88%, respectively, in women aged 40 or less and those over the age of 40 [Abramovich et al., 1995].

Of course, endometrial ablation success or failure depends on several factors. Furthermore, treatment failure is more likely after a repeat ablation than after a first ablation [Erian, 1994; HTAC, 2000]. The actual and perceived severity of the symptoms, the woman's expectations, and the presence of a uterine disease causing bleeding all seem to play a role. The other factors are the intrinsic efficacy of the surgical procedure, the surgeon's skill and the scarring process of the uterus [Davis et al., 1998; Parkin, 1998; Parkin, 2000a]. However, even if the prognostic factors are known, the outcome of an endometrial ablation in a given patient cannot be predicted with certainty [Parkin, 1998; Parkin, 2000a].

4.2.4.3 Effects and postoperative complications

The bleeding following an endometrial ablation lasts approximately nine days. This is followed by a watery, bloody discharge that lasts an average of 14 days [Garry, 1995b; HTAC, 2000].

One of the drawbacks of endometrial ablation is the risk of persistent or recurrent dysfunctional uterine bleeding, which requires a repeat ablation or possibly a hysterectomy. A systematic review revealed that the risk of reintervention following failure of the initial surgical treatment was significantly higher in cases of endometrial ablation than in cases of hysterectomy throughout the follow-up, in other words, during the first (odds ratio[2] [OR]: 7.33; 95% confidence interval [CI]: 4.18 to 12.86), the second (OR: 7.50; 95% CI: 4.20 to 13.42), the third (OR: 4.45; 95% CI: 1.78 to 11.15) and fourth (OR: 9.84; 95% CI: 4.92 to 19.67) year after the initial procedure [Lethaby et al., 2000d]. In a randomized clinical study, repeat surgery was necessary in 38% of the women who had undergone endometrial ablation (laser ablation or transcervical resection) at least once because of persistent or recurrent dysfunctional bleeding during the four years following the initial operation. The cumulative probability of reintervention (repeat ablation or hysterectomy) was 36% and 40%, respectively, after four and five years. The probability of hysterectomy was 24% and 30%, respectively, for the same periods [Grant et al., 1999]. The results of another study suggest that there is a linear relationship between the cumulative incidence of hysterectomy and time from endometrial ablation in the first five years [Unger and Meeks, 1996].

A retrospective study was carried out for the purpose of determining the 5-year cumulative incidence of hysterectomy after endometrial ablation for dysfunctional uterine bleeding [Sylvestre et al., 2000]. A chart review was done on 218 patients operated on by five gynecologists at the Saint-Sacrement Branch of the Centre hospitalier affilié universitaire de Québec. Two endometrial ablation techniques had been used: transcervical resection (with treatment of the cornual regions and the uterine fundus with a rollerball electrode) and rollerball ablation. The cumulative incidence of hysterectomy was 5.9%, 8.3%, 12.3%, 17.5% and 18.6%, respectively, 12, 24, 36, 48 and 60 months after the initial intervention. The interval between the initial ablation and the hysterectomy ranged from 0 to 74 months, with a mean interval of 26.5 ± 19.8 months. Only age had a statistically significant influence on the probability of hysterectomy. The cumulative incidence of hysterectomy 60 months after the initial operation was 53.4% and 11.6%, respectively, in the women aged 35 or less and those over the age of 35. The relative risk[3] of hysterectomy being performed after endometrial ablation in the women over the age of 35 was 0.19 (comparison with the women aged 35 or less; 95% CI: 0.09 to 0.38).

Pregnancy is rare but possible after endometrial ablation, even in amenorrheic women [Garry, 1995b; HTAC, 2000; Holt and Gillmer, 1995; Kammerer-Doak and Rogers, 2000; Ke, 1997]. Such pregnancy can be difficult to diagnose and carries certain risks. The risk of ectopic pregnancy is considerably higher. Even if the embryo attaches to and successfully implants in the endometrium, possible complications include a decreased blood supply to the uterus, which can cause impaired fetal growth and impaired placentation [Garry, 1995b; HTAC, 2000].

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[2] Calculated using the Peto method.

[3] Calculated using the Cox adjusted-regression model.

It is possible for endometrial cancer to develop in residual endometrium after an ablation, not because of the procedure itself, but because of the risk of adenocarcinoma to which all women are exposed. Such cancer can be difficult to diagnose because of the presence of scar tissue in the uterus. In fact, the scarring and intrauterine contractures caused by a complete endometrial ablation could block the uterine bleeding that might occur after possible regeneration of endometrial cells and delay the diagnosis of endometrial cancer. However, this hypothesis has not yet been proven [McCausland and McCausland, 1999a; McCausland and McCausland, 1999b]. The effects of hormone replacement therapy on residual endometrium in postmenopausal women are still unknown [Garry, 1995b; HTAC, 2000; Ke, 1997]. Any woman who undergoes an endometrial ablation and who is on hormone replacement therapy should receive an estrogen-progestin combination and be considered as if she had not had an endometrial ablation[4].

4.2.4.3.1 Specific complications of hysteroscopic endometrial ablation

The mechanical complications of hysteroscopic endometrial ablation include cervical laceration and uterine perforation. Large uterine perforations may require a laparotomy to rule out extensive injury or bleeding [Cooper and Brady, 1999; Garry, 1995b; HTAC, 2000; Holt and Gillmer, 1995]. This is because potentially serious complications can occur if a perforation goes undetected and if a laparotomy or laparoscopy is not performed immediately, especially if the ablation was performed by laser or resectoscope. In such circumstances, the small or large intestine can be injured by the conduction of electrical current or by direct exposure to the laser beam. Untreated bowel damage can be fatal [Baggish, 1992; Cooper and Brady, 1999; Garry, 1995b; HTAC, 2000].

The media used to distend the uterine cavity during hysteroscopy can cause fluid overload, allergic reactions and other toxic reactions. Fluid overload is associated with unduly long operating times, the use of too high a distending pressure, and the resection of large myomas during the operation. An overload of hypotonic irrigation solution can cause increased central venous pressure and hyponatremia which, if untreated, can lead to pulmonary edema, hypotension, cerebral edema and potentially fatal cardiovascular collapse [Baggish, 1992; Cooper and Brady, 1999; Garry, 1995b; HTAC, 2000; Holt and Gillmer,1995; Ke, 1997].

To avoid these complications, irrigation fluid use must be closely monitored during the procedure and the patient observed for any signs or symptoms of excessive fluid absorption. Most physicians will stop a hysteroscopic procedure if the collector shows a 1- to 1.5-liter fluid deficit, when using glycine, sorbitol or mannitol, to avoid hyponatremic hypervolemia. A lower threshold may be necessary in older patients or those with preexisting cardiovascular problems. Dextran 70 has been associated with fluid overload, pulmonary edema, intravascular coagulopathy, renal failure and rhabdomyolysis, as well as anaphylactoid reactions. Glycine can result in hyperammonemic encephalopathy, and transient blurred vision and blindness [Cooper and Brady, 1999; Garry, 1995b; HTAC, 2000; Ke, 1997].

Uterine hemorrhage can occur if the ablation extends too deeply into the myometrium and large blood vessels are cut [Cooper et Brady, 1999; Garry, 1995b; HTAC, 2000]. Intraoperative hemorrhage can be treated by aspirating the blood and raising the distending pressure to above the blood pressure so as to sufficiently compress the walls of the uterus to control the bleeding. This can, however, lead to the absorption of a large quantity of irrigation fluid and to serious complications. It is therefore preferable to cauterize the severed blood vessels as soon as possible [HTAC, 2000]. Hemorrhage can also result from releasing the pressure exerted by the irrigation fluid at the end of the surgical procedure [Baggish, 1992]. In such cases, local compressive hemostasis using a balloon catheter is the treatment of choice [Baggish, 1992; Cooper and Brady, 1999; Garry, 1995b; HTAC, 2000].

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[4] Written communication from R. Sabbah, M.D., Hôpital du Sacré-Cœur de Montréal, December 2001.

Air embolism is a rare, potentially fatal complication of operative hysteroscopy [Baggish, 1992; Cooper and Brady, 1999; Garry, 1995b; HTAC, 2000]. It may occur when venous sinuses on the surface of the endometrium are opened and exposed to ambient air. Factors that predispose to air embolism include the Trendelenburg position and cervical trauma [Cooper and Brady, 1999; Garry, 1995b; HTAC, 2000].

Two surveys in Scotland and the United Kingdom showed that hysteroscopic endometrial ablation is associated with a relatively low incidence of intraoperative complications [Abramovich et al., 1995; Overton et al., 1997]. The Scottish survey included a prospective study of the effectiveness and complications of nearly 1,000 endometrial ablations performed between December 1991 and December 1993 [Abramovich et al., 1995]. Laser ablation was performed in close to one-third of the women (32%), transcervical resection in 65% of the women and rollerball ablation in the remaining 3%. The total incidence of intraoperative complications was found to be 12%. The complications included fluid overload (more than 2 L), uterine perforation, hemorrhage and emergency laparoscopy or emergency hysterectomy (after uterine rupture), these in, respectively, 1.0%, 1.1%, 3.6% and 1.2% of the participants. One patient died, perhaps of toxic shock syndrome, after uncomplicated transcervical resection (1 case out of 629 resections, or 0.16%). Statistically, there is no evidence of a link between the incidence of intraoperative complications and the surgeon's experience. Reintervention was necessary in 23.9% of the women, with 12.6% of these women undergoing a repeat ablation, the remaining 11.3% undergoing a hysterectomy. No difference was observed between the various procedures in terms of complications (with the exception of fluid overload) or efficacy.

The prospective survey conducted in the United Kingdom (the MISTLETOE study) involved a detailed examination of clinical data on more than 10,000 women [Overton et al., 1997]. For hysteroscopic endometrial ablation techniques, the authors report a total incidence of intraoperative complications of 4.44%. Specifically, they report fluid overload (more than 2 L), uterine perforation, hemorrhage and emergency reintervention in 1.9%, 1.5%, 2.4% and 1.25% of the participants, respectively. The number of postoperative complications associated with the four main techniques was extremely low. These results indicate that hysteroscopic ablation techniques are safe, even when the surgeon is inexperienced [Lethaby et al., 2000d; Overton et al., 1997; Parkin, 2000a].

Two smaller studies report complication rates as well. In one of these studies, a prospective, multicentre trial involving 494 hysteroscopic endometrial ablations, the incidence of complications was 0.8%, with perforation of the uterine cavity being the most frequent complication (0.6%) [Jansen et al., 2000]. In close to half the cases, the perforation occurred upon insertion of the resectoscope. Fluid overload occurred in 0.2% of the patients. In the other study, hysteroscopic endometrial ablation entailed fewer intraoperative complications than the other types of operative hysteroscopies (OR: 0.4; 95% CI: 0.1 to 3.3) [Propst et al., 2000]. Fluid overload occurred in 1.3% of the patients.

5

EFFICACY AND SAFETY OF ENDOMETRIAL ABLATION TECHNIQUES IN THE TREATMENT OF DYSFUNCTIONAL UTERINE BLEEDING

The results of the main uncontrolled clinical studies of the efficacy and safety of endometrial ablation techniques are presented in Appendix C. The results of three randomized, controlled trials of endometrial ablation with and without pretreatment with endometrial thinning agents, are included as well.

5.1 First-generation ablation techniques

The instruments used in photocautery, electrocautery and electrocoagulation of the endometrium include a light source and a hysteroscope, a uterine distension system and an energy source and ablative attachments. A video camera connected to a display monitor can also be used to enhance visualization of the interior of the uterine cavity [Garry, 1995b; HTAC, 2000; Kammerer-Doak and Rogers, 2000].

In order for the surgeon to adequately visualize the entire uterine cavity, it must be distended by instilling a liquid. Operative hysteroscopy is usually performed with low-viscosity fluids that continuously flow into and out of the uterus, clearing out blood and debris and improving the surgeon's field of view. Glycine and sorbitol solutions are two of the irrigation fluids used more often during endometrial ablation. A distending pressure of 80 to 110 mm Hg ensures optimal distention and continuous irrigation. The quantity of fluid instilled and recovered is measured every five minutes [Garry, 1995b; HTAC, 2000; Holt and Gillmer, 1995; Kammerer-Doak and Rogers, 2000].

The first-generation techniques are usually performed under general anesthesia but can also be performed with local or regional anesthesia [Garry, 1995b; HTAC, 2000; Holt and Gillmer, 1995; Ke, 1997]. The hysteroscope is inserted through the cervix, and its sheath is flushed with irrigation fluid. Manipulating the hysteroscope and sheath, the physician examines the entire uterine cavity before ablation begins [Garry, 1995b; HTAC, 2000; Ke, 1997].

5.1.1 Laser ablation

This type of photocautery of the endometrium is performed with a laser inserted, with hysteroscopic guidance, into the uterus for the purpose of destroying the endometrium. During the ablation process, submucous fibroids and polyps can be destroyed as well [Kammerer-Doak and Rogers, 2000]. Laser ablation usually takes about 20 to 35 minutes [HTAC, 2000; Ke, 1997]. It seems that laser ablation stopped being performed in Québec about 10 years ago[5].

There have been many large, uncontrolled published clinical studies of the efficacy and safety of laser ablation in the treatment of dysfunctional uterine bleeding (see Table C.1). The results of studies that compared laser ablation with other ablation techniques have been published as well and are presented later in this report.

In the uncontrolled studies, laser ablation resulted in amenorrhea rates ranging from 23.0 to 81.4%, markedly reduced or normalized menstrual blood loss in 18.6 to 77.0% of the women, and unchanged or even increased menstrual flow in 0 to 8.6% of the cases examined [Baggish and Sze, 1996; Bernhard, 1994; Erian, 1994; Everett, 1999; Garry et al., 1991; Garry et al., 1995; Gimpelson, 1988; Goldfarb, 1990; Goldrath, 1990; Lomano et al., 1986; Phillips et al., 1998]. Although not reported by all of the authors, the satisfaction rate varied from 83.4 to 97.3% [Bernhard, 1994; Garry et al., 1991; Garry et al., 1995; Phillips et al., 1998].

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[5] Written communication from P.Y. Laberge, M.D., CHUQ Research Centre, November 2001.

The duration of follow-up ranged from 3 months to 11 years. During the posttreatment follow-up, 1.5 to 14.3% of the women required a repeat ablation (0.2 to 0.6% of them had to undergo a third ablation) and 0 to 14.6% required a hysterectomy [Bernhard, 1994; Erian, 1994; Everett, 1999; Garry et al., 1991; Garry et al., 1995; Gimpelson, 1988; Goldfarb, 1990; Goldrath, 1990; Lomano et al., 1986; Phillips et al., 1998]. In addition, an analysis of the survival curve indicated that 21% of laser-treated women will require a hysterectomy during the 6.5 years following the initial intervention [Phillips et al., 1998].

The complication rates reported in uncontrolled studies range from 0.8 to 29.2%. Potentially serious complications of laser ablation included uterine perforation (0 to 1.6%), fluid overload (0 to 5.0%) and hemorrhage (0 to 3.9%). Furthermore, the retention of menstrual blood (hematometra) or the discharge of pus from the uterus (pyometra), associated with scarring and obliteration of the endocervical canal and concurrent with continuous bleeding from residual endometrium, could occur as well. The other complications reported included infection, pyrexia, endometritis or myometritis, cervical bleeding, pregnancy, vaginitis and DVT [Baggish and Sze, 1996; Bernhard, 1994; Erian, 1994; Everett, 1999; Garry et al., 1991; Garry et al., 1995; Gimpelson, 1988; Goldfarb, 1990; Goldrath, 1990; Lomano et al., 1986; Phillips et al., 1998]. In addition, three reports have been published of cases of bowel injury due to uterine perforation [Perry et al., 1990].

The main drawbacks of laser endometrial ablation are that it is more expensive and takes longer than the electrosurgical techniques [Kammerer-Doak and Rogers, 2000]. Furthermore, some fear endometrial cancer going undetected due to the lack of endometrial tissue for a postoperative histopathological examination [Garry et al., 1995; HTAC, 2000]. Even if the uterine cavity seems normal on hysteroscopic examination, a small piece of the endometrium should be removed, since hysteroscopy alone cannot rule out the possibility of neoplasm or endometrial carcinoma [Vilos et al., 2001].

5.1.2 Transcervical resection

This type of electrocautery of the endometrium is performed with a resectoscope at whose tip is a metal loop supplied with high-frequency electrical current. If the surgeon has difficulty reaching the cornual regions with the metal loop, a rollerball electrode can be used to destroy the endometrium in these regions by electrocoagulation. This technique is sometimes referred to as "combined diathermy". Transcervical resection takes about 15 to 20 minutes.

Tables C.1 and C.2 in Appendix C show the results of the main uncontrolled clinical studies of the efficacy and safety of transcervical resection in the treatment of dysfunctional uterine bleeding and those of a randomized trial that evaluated transcervical resection depending upon whether or not it was preceded by endometrial thinning with pharmacological agents. The results of studies that compared transcervical resection and hysterectomy or other endometrial ablation techniques have been published as well and are presented later in this report.

In the uncontrolled trials, transcervical resection resulted in amenorrhea rates ranging from 8.0 to 94.4%, markedly reduced or normalized menstrual blood loss in 5.6 to 75.5% of the women, and unchanged or even increased menstrual flow in 0 to 28.0% of the cases examined [Browne, 1996; DeCherney et al., 1987; Maher and Hill, 1990; Magos et al., 1991; O'Connor and Magos, 1996; Pyper and Haeri, 1991; Salat-Baroux et al., 1996; Senden and Brooks, 1991; Steffensen and Schuster, 1997; Yin et al., 1998]. Although not reported by all of the authors, the satisfaction rate varied from 63 to 100% [Magos et al., 1991; O'Connor and Magos, 1996; Rankin and Steinberg, 1992; Steffensen and Schuster, 1997; Yin et al., 1998].

Follow-up ranged from 3 months to 5 years. During the posttreatment follow-up, 2.0 to 17.5% of the women required a repeat ablation (0.3 to 1.3% of them had to undergo a third ablation) and 0 to 9.0% required a hysterectomy [DeCherney et al., 1987; Maher and Hill, 1990; Magos et al., 1991; O'Connor and Magos, 1996; Pyper and Haeri, 1991; Rankin and Steinberg, 1992; Salat-Baroux et al., 1996; Steffensen and Schuster, 1997; Yin et al., 1998].

The complication rates reported in the uncontrolled studies ranged from 0 to 17.2%. Complications such as uterine perforation (0 to 3.8%), with or without injury to the pelvic viscera, fluid overload (0 to 3.8%) and hemorrhage (0 to 14.3%) were most often due to surgical inexperience and to the use of a metal loop instead of a rollerball electrode in the cornual regions and uterine fundus [DeCherney et al., 1987; Maher and Hill, 1990; Magos et al., 1991; O'Connor and Magos, 1996; Pyper and Haeri, 1991; Rankin and Steinberg, 1992; Salat-Baroux et al., 1996; Senden and Brooks, 1991; Steffensen and Schuster, 1997; Yin et al., 1998]. Intraoperative and postoperative hemorrhage is rare but can occur, mainly in cases of deep injury to the myometrium. A visual inspection of the newly resected uterine cavity and coagulation of the bleeding points will serve to ensure hemostasis and reduce the risk of hemorrhage [Dwyer et al., 1993; Gannon et al., 1991; Ke, 1997]. The other complications reported included hematometra, secondary hemorrhage, cervical laceration, cervical stenosis, endometritis, infection, unexpected malignant tumor, pregnancy and febrile syndrome [Maher and Hill, 1990; Magos et al., 1991; O'Connor and Magos, 1996; Pyper and Haeri, 1991; Rankin and Steinberg, 1992; Salat-Baroux et al., 1996; Steffensen and Schuster, 1997; Yin et al., 1998].

Two randomized trials were conducted to compare the efficacy and safety of transcervical resection preceded by endometrial thinning with pharmacological agents and transcervical resection without pretreatment of the uterus [Kriplani et al., 2002; Rai et al., 2000]. One of these studies showed that preoperative endometrial thinning is beneficial, as it reduces fluid absorption and the duration of surgery and improves the operating conditions [Kriplani et al., 2002]. No statistically significant difference was observed between the women who had undergone preoperative endometrial thinning and those who had not. Similarly, no significant difference was noted in any of the groups with regard to the level of satisfaction with the surgical intervention. The authors do not report the results of the statistical analysis concerning the need to provide further treatment [Rai et al., 2000]. The fact that no difference was observed for most of the study variables in these trials might be due to the small study samples. These results would therefore need to be confirmed in a large, multicentre clinical trial.

The advantages of transcervical resection over laser or rollerball ablation include the possibility of performing an endometrial biopsy in order to rule out the presence of a neoplasm and the possibility of surgically removing benign intrauterine tumors, such as polyps and leiomyomas. On the other hand, it requires a high level of surgical skill and carries a greater risk of uterine perforation and systemic absorption of irrigation fluid as a result of blood vessel exposure [Garry, 1995b; Kammerer-Doak and Rogers, 2000]. Of the contraindications to this technique, particular mention should be made of hemodynamic instability, coagulopathies and anticoagulant therapy.

5.1.3 Rollerball ablation

Rollerball ablation is similar to transcervical resection. However, this type of electrocoagulation of the endometrium is performed with a resectoscope at whose tip is a spherical metal part (rollerball) supplied with high-frequency electrical current. Rollerball ablation takes about 15 to 30 minutes. This technique was used for the first time by Dr. Vancaillie, who, at the time, lived in the United States [Vancaillie, 1989]. Most gynecologists in North America who perform endometrial ablations use the rollerball technique[6].

The results of 12 uncontrolled clinical studies of the efficacy and safety of rollerball ablation in the treatment of dysfunctional uterine bleeding have been published (see Table C.4). The results of studies that compared rollerball ablation with hysterectomy or other endometrial ablation techniques have been published as well and are presented later in this report.

In the uncontrolled trials, rollerball ablation resulted in amenorrhea rates ranging from 25.0 to 60.0%, markedly reduced or normalized menstrual blood loss in 35.0 to 69.0% of the women, and unchanged or even increased menstrual flow in 0 to 16.2% of the cases examined [Alford and Hopkins, 1996; Baggish and Sze, 1996; Chullapram et al., 1996; Daniell et al., 1992; Dutton et al., 2001; El Senoun et al., 2000; Fraser et al., 1993; Paskowitz, 1995; Teirney et al., 2000; Vilos et al., 1996b; Wortman and Daggett, 1993]. Although not reported by all of the authors, the satisfaction rates were comparable, varying from 78.8 to 87.8% [Chullapram et al., 1996; Daniell et al., 1992; El Senoun et al., 2000; Unger and Meeks, 1996].

Follow-up ranged from 0.25 months to 11 years. During the posttreatment follow-up, 0 to 11.5% of the women required a repeat ablation and 1.4 to 34.1% required a hysterectomy [Alford and Hopkins, 1996; Chullapram et al., 1996; Daniell and al., 1992; Dutton et al., 2001; El Senoun et al., 2000; Fraser et al., 1993; Paskowitz, 1995; Teirney et al., 2000; Unger and Meeks, 1996; Vilos et al., 1996b; Wortman and Daggett, 1993]. An analysis of the survival curve showed that 71% (95% CI: 51 to 86) of women treated by rollerball ablation will not require a hysterectomy during the first five years following the initial intervention [Dutton et al., 2001].

The complication rates reported in the uncontrolled studies ranged from 0 to 8.3%. Potentially serious complications of rollerball ablation included uterine perforation (0 to 4.3%), fluid overload (0 to 2.6%) and hemorrhage (0 to 1.3%). The other complications reported included infection, persistent postoperative pain, endometritis or myometritis, salpingitis, intrauterine pregnancy, cervical stenosis, tubo-ovarian abscesses and leiomyosarcoma [Alford and Hopkins, 1996; Baggish and Sze, 1996; Daniell et al., 1992; Dutton et al., 2001; El Senoun et al., 2000; Fraser et al., 1993; Paskowitz, 1995; Unger and Meeks, 1996; Vilos et al., 1996b; Wortman and Daggett, 1993]. There are also three published reports of cases of genital tract burns (cervix, vagina, vulva) [Vilos et al., 1997a].

Rollerball ablation carries a lower risk of uterine perforation and fluid absorption because the tip of the rollerball is blunt. It is easier to master from a technical standpoint and quicker to perform than laser ablation and transcervical resection [Kammerer-Doak and Rogers, 2000; Overton et al., 1997]. Rollerball ablation is especially indicated for uterine bleeding secondary to anticoagulant therapy. Even if the uterine cavity seems normal on hysteroscopic examination, a small piece of the endometrium should be removed, since hysteroscopy alone cannot rule out the possibility of neoplasm or endometrial carcinoma [Vilos et al., 2001]. Although rollerball ablation compares with laser ablation or transcervical resection in terms of the amenorrhea rate, fewer women indicated that they were amenorrheic as the posttreatment follow-up proceeded [Baggish and Sze, 1996; Chullapram et al., 1996; Daniell et al., 1992; El Senoun et al., 2000; Fraser et al., 1993; Kammerer-Doak and Rogers, 2000; Vilos et al., 1996b].

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[6] Written communication from P.Y. Laberge, M.D., CHUQ Research Centre, November 2001.

5.2 Second-generation ablation techniques

The second-generation endometrial ablation techniques can be performed under general anesthesia, with local anesthesia (with or without intravenous sedation) or under narcosis. Most manufacturers attempt to market these techniques as procedures that can be performed on an outpatient basis [Jones et al., 2000]. It is important that physicians and patients be aware of the diameter of the device to be inserted into the uterus [Cooper and Erickson, 2000].

Given that these new techniques are performed without visual hysteroscopic monitoring (with the exception of hydrothermal endometrial ablation), the physician should make a diagnosis based on a visual examination prior to treatment, as well as a diagnosis supported by a pathophysiological study which includes a hysteroscopy and, at the very least, an endometrial biopsy[7]. It is also advisable to perform a hysteroscopy after the treatment to check that only the uterine cavity was treated [Vilos et al., 2001].

When this report was being drafted, five second-generation techniques had been the subject of rigorous assessments involving a comparison with established techniques. Only microwave ablation and impedance-controlled ablation had been compared with the standard conventional therapy, transcervical resection. In the case of thermal balloon ablation, hydrothermal ablation and cryoablation, the comparator technique was rollerball ablation. Unfortunately, searches in the computerized literature databases did not yield any published randomized, controlled trials of endometrial laser intrauterine thermotherapy. Given the paucity of published data, this technique was not included in our assessment and is only briefly described in appendix B.

5.2.1 Microwave ablation

5.2.1.1 Microwave Endometrial Ablation™ System

Development of the Microwave Endometrial Ablation (MEA™) System began in the United Kingdom in 1993 at the University of Bath School of Physics. The first experimental trials were conducted in collaboration with the Department of Medical Physics and the Directorate of Gynecology at the Bath Royal United Hospital [Hodgson et al., 1999; Sharp et al., 1998]. The clinical trials began in October 1994.

An 8-mm-diameter circular waveguide transmits electromagnetic energy at a frequency of 9.2 gigahertz (GHz). The cervix has to be dilated to 9 mm in order to insert the waveguide up to the uterine fundus. Microwaves travel through the hand-held applicator and are guided to the tip, where they are absorbed by the surrounding endometrium. The microwaves, which are emitted from the applicator tip in a hemispherical pattern, diminish by 90% at a depth of about 3 mm. Tissue outside this area of intense heating is destroyed by the conduction of thermal energy at a distance from the heated area. The microwaves do not, therefore, penetrate the myometrium or exit the uterus. Microwave ablation takes between 1 and 7 minutes, depending on the size of the uterus [Hodgson et al., 1999; Sharp et al., 1998; Sharp et al., 2000].

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[7] Written communication from R. Sabbah, M.D., Hôpital du Sacré-Cœur de Montréal, December 2001.

The results of a few uncontrolled clinical studies of the efficacy and safety of microwave ablation (MEA) in the treatment of dysfunctional uterine bleeding have been published (see Table C.5). The results of a randomized trial that compared this technique (MEA) and transcervical resection of the endometrium have been published as well and are presented later in this report.

In the uncontrolled trials, microwave ablation resulted in amenorrhea rates ranging from 18.8 to 56.5%, markedly reduced or normalized menstrual blood loss in 26.1 to 74.9% of the women, and unchanged or even increased menstrual flow in 6.3 to 17.4% of the cases examined. Although not reported by all of the authors, the satisfaction rates were comparable, varying from 82.2 to 87.5% [Hodgson et al., 1999; Milligan and Etokowo, 1999; Sharp et al., 2000].

Follow-up ranged from 6 months to 2 years. During the posttreatment follow-up, 0 to 13% of the women required a repeat ablation and 0 to 11% required a hysterectomy [Hodgson et al., 1999; Milligan and Etokowo, 1999; Sharp et al., 1995; Sharp et al., 2000].

The complication rates reported in the uncontrolled studies ranged from 1.2 to 25.1%. The only potentially serious complication of microwave ablation was uterine perforation (0 to 0.3%). The other complications reported included endometritis, urinary tract infection, purulent vaginal discharge and intense postoperative pain requiring hospitalization and analgesia [Hodgson et al., 1999; Milligan and Etokowo, 1999; Sharp et al., 2000].

A large body of data on the safety of this technique has been published [Parkin, 2000b]. In one study, 1,433 microwave ablations (MEA) performed at 13 gynecology units in the United Kingdom and Canada were examined. The complication rate was extremely low (1.46%). There were no cases of emergency hysterectomy following microwave ablation. Perforation of the small intestine was the only serious complication to occur, and this in one patient (0.07%) who had previously had two cesareans. The perforation was probably caused by thermal injury following false passage. The patient had a satisfactory recovery. There were four cases of blunt trauma (0.28%), three of which occurred during systematic dilatation with a Hegar dilator and one upon insertion of the applicator into a retroverted uterus that had been difficult to dilate. Two women (0.14%) experienced intense pain. In both cases, the pain did not yield to the administration of opioids [Parkin, 2000b]. These women were brought back to the operating room, where they were given local intracervical anesthesia, which provided immediate relief [Sharp et al., 1998]. The article also indicates that the incidence of mild complications, such as endometritis, was very low (1%) [Parkin, 2000b].

Tulandi and Felemban conducted a prospective study in which they evaluated the appearance of the uterine cavity before and after microwave ablation (MEA) [Tulandi and Felemban, 2001]. Endometrial ablation was successfully completed in 55 of the 62 women. Although it was incomplete in 7 patients, about 90% of the uterine mucosa had been destroyed, with only a small island of intact endometrium remaining. The uterine cavity was severely distorted in six of these women, and a seventh had an acutely retroverted uterus (tipped backward).

In addition, the uterine cavities of these women were larger than those of the women in whom the ablation was successfully completed (respectively, 101.4 ± 15.5 mm and 84.7 ± 12.8 mm; $P = 0.008$). Although the authors conclude that microwave ablation tends to be incomplete in women with a large and severely deformed uterine cavity, whether residual endometrium results in a lower surgical success rate remains to be demonstrated. It should be noted that the cervix has to be dilated to 9 mm in order to insert the waveguide and that the dilatation process can be painful, even with local anesthesia.

5.2.2 Thermal balloon ablation

The following thermal balloon ablation systems have been developed: ThermaChoice™ II, Cavaterm™ plus and MenoTreat™. Destruction of the endometrium and the superficial myometrium with these devices is achieved through a combination of heat and pressure in the uterine cavity. The cervix has to be dilated in order to insert the Cavaterm plus or MenoTreat catheter up to the uterine fundus. Given their distensibility, the balloons should fit the shape of the uterine cavity [Parkin, 2000a].

The use of these devices with local anesthesia causes pain because of the uterine distention. Furthermore, since it also seems to be reserved for normal uterine cavities, at least 30% of endometrial ablation candidates cannot avail themselves of this technique, as witnessed by the results of the Scottish survey on hysteroscopic interventions [Abramovich et al., 1995; Parkin, 2000a].

The efficacy and safety of the Cavaterm plus System and MenoTreat System have not been established in randomized, controlled trials. Consequently, the results of the few uncontrolled clinical trials published to date will not be presented in this report [Alaily, 1998; De Grandi and El Din, 2000; Friberg et al., 1998; Friberg and Ahlgren, 1998; Friberg and Ahlgren, 2000; Genolet et al., 1999; Hawe et al., 1999; Ulmsten et al., 2001; Wirz et al., 1998]. These two systems are briefly described in appendix B. As at July 31, 2002, the MenoTreat had not been approved by Canada's Health Products and Food Branch (HPFB).

5.2.2.1 ThermaChoice™ Uterine Balloon Therapy™ System

Originally, the balloon was made of latex. Improvements have since been made to this device. The ThermaChoice II now includes a new silicone balloon and a fluid mixing element housed inside the catheter that circulates lukewarm fluid and ensures constant temperatures throughout the procedure. The catheter is 16 cm long and 4.5 mm in diameter.

The single-use balloon catheter is advanced through the cervix to the uterine fundus, then filled with a heated fluid that coagulates the endometrium. A heating element inside the balloon heats the fluid to 87°C for 8 minutes [Amso et al., 1998; Bongers et al., 2002; Brun et al., 2000; Cooper and Erickson, 2000; HTAC, 2000; Meyer et al., 1998].

Nine uncontrolled clinical studies have examined the efficacy and safety of thermal balloon endometrial ablation (ThermaChoice) in the treatment of dysfunctional uterine bleeding, and one randomized, controlled trial has evaluated the efficacy of this technique depending upon whether or not it is preceded by endometrial thinning with pharmacological agents (see Tables C.6 and C.7). The results of three controlled studies, including a randomized trial, of thermal balloon ablation (ThermaChoice) and rollerball ablation or transcervical resection have been published as well and are presented later in this report.

In the uncontrolled trials, thermal balloon ablation resulted in amenorrhea rates ranging from 3.3 to 54.5%, markedly reduced or normalized menstrual blood loss in 44.4 to 76.9% of the women, and unchanged or even increased menstrual flow in 0 to 23.3% of the cases examined [Aletebi et al., 1999; Amso et al., 1998; Bongers et al., 2002; Buckshee et al., 1998; Fernandez et al., 1997; Singer et al., 1994; Vilos et al., 1996c; Vilos et al., 2000]. In one of these studies, the treatment failure rate increased from 16.7% six months after the initial intervention to 23.3% during the period from 12 to 18 months after the initial operation [Vilos et al., 1996c]. In general, the level of satisfaction with the treatment was not determined in these studies. In fact, only two articles report satisfaction rates; they range from 81.0 to 84.6% [Bongers et al., 2002; Buckshee et al., 1998].

The duration of follow-up ranged from 2 to 34 months. During that time, 0 to 36.7% of the women required a repeat ablation and 0 to 15.4% required a hysterectomy [Aletebi et al., 1999; Amso et al., 1998; Bongers et al., 2002; Buckshee et al., 1998; Fernandez et al., 1997; Singer et al., 1994; Vilos et al., 1996c; Vilos et al., 1997b].

The complication rates reported in these uncontrolled studies ranged from 0 to 15.4%. No potentially serious complications were reported [Aletebi et al., 1999; Amso et al., 1998; Buckshee et al., 1998; Fernandez et al., 1997; Lissak et al., 1999; Singer et al., 1994; Vilos et al., 1996c; Vilos et al., 1997b; Vilos et al., 2000]. The complications reported included mild abdominal cramps, endometritis, hematometra, urinary tract infection, bradycardia and intense postoperative pain [Amso et al., 1998; Buckshee et al., 1998; Lissak et al., 1999; Singer et al., 1994; Vilos et al., 1997b]. Although the studies published thus far make no mention of it, just one case of uterine perforation occurred in the approximately 3,000 women treated by thermal balloon ablation (ThermaChoice) worldwide [FDA, 1997].

A randomized trial compared the efficacy and safety of thermal balloon ablation (ThermaChoice) without pretreatment with endometrial thinning agents and delayed ablation after such pretreatment in perimenopausal women with dysfunctional uterine bleeding [Lissak et al., 1999]. During the 6-month posttreatment follow-up, no significant difference was observed between the women treated with immediate or delayed ablation in terms of menstrual flow patterns or the duration (measured in days) of blood loss per cycle. As well, no significant difference was noted with regard to the participants' satisfaction with the procedure. However, the authors do not provide the results of the statistical analysis concerning the need for further treatment. The fact that no significant differences were observed for most of the study variables might be due to the small study sample, for the results of a prospective study involving 130 women indicate that the risk of treatment failure might be greater when the pretreatment endometrial thickness is 4 mm or more [Bongers et al., 2002]. These findings would therefore need to be confirmed in a large, multicentre clinical trial.

Among the contraindications to thermal balloon ablation (ThermaChoice), particular mention should be made of an active genital or urinary tract infection or any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy [FDA, 1997]. Uterine retroversion is associated with a higher risk of treatment failure [Bongers et al., 2002].

5.2.3 Hydrothermal ablation

The following two systems have been designed for hydrothermal ablation: the Hydro ThermAblator® and the EnAbl™. The destruction of the endometrium and superficial myometrium with these devices is based on the instillation and circulation of heated normal saline inside the uterine cavity.

The efficacy and safety of the EnAbl System have not been demonstrated in any published randomized, controlled trials. Furthermore, a search in the computerized literature databases did not yield any published uncontrolled clinical studies. The EnAbl is briefly described in appendix B. As at July 31, 2002, it had not been approved by the HPFB.

5.2.3.1 Hydro ThermAblator® Endometrial Ablation System

The microprocessor unit in the Hydro ThermAblator (HTA®) is connected to a single-use, 7.8-mm-diameter, insulated sheath into which a 3.0-mm, standard hysteroscope is inserted [Römer and Müller, 1999; Weisberg et al., 2000]. The cervix has to be dilated to 8 mm in order to insert the sheath. The sheath is inserted into the uterine cavity under hysteroscopic visualization, then the cavity is irrigated with room-temperature normal saline. The cavity is then rinsed and distended to permit visual confirmation that the sheath is properly in place and detection of any intrauterine pathology not previously diagnosed. The saline, which is constantly circulating, is then heated to the preset temperature of 90°C. At this temperature, the entire thickness of the endometrium is destroyed. The treatment takes 10 minutes [Cooper and Erickson, 2000; das Dores et al., 1999; Goldrath et al., 1997; Richart et al., 1999; Römer and Müller, 1999; Weisberg et al., 2000].

The results of a few uncontrolled clinical studies of the efficacy and safety of hydrothermal ablation (HTA) in the treatment of dysfunctional uterine bleeding have been published (see Table C.8). The results of a randomized trial that compared hydrothermal ablation (HTA) and rollerball ablation have been published as well and are presented later in this report.

In the uncontrolled trials, hydrothermal ablation resulted in amenorrhea rates ranging from 32.0 to 84.6%, markedly reduced or normalized menstrual blood loss in 15.4 to 64.0% of the participants, and unchanged or even increased menstrual flow in 0 to 14.0% of the cases examined [das Dores et al., 1999; Perlitz et al., 2001; Römer et Müller, 1999; Römer et al., 2000; Weisberg et al., 2000]. Although not reported by all of the authors, the satisfaction rates were comparable, varying from 92.3 to 96.0% [das Dores et al., 1999; Perlitz et al., 2001; Römer et Müller, 1999].

The duration of follow-up ranged from 3 to 18 months. During the posttreatment follow-up, 0 to 7.7% of the women required a repeat ablation and 3.8 to 7.1% required a hysterectomy [das Dores et al., 1999; Perlitz et al., 2001; Römer et Müller, 1999; Weisberg et al., 2000].

The complication rates reported in the uncontrolled studies ranged from 0 to 25.0%. No potentially serious complications with hydrothermal ablation were reported. The complications reported included vaginal burns, abdominal cramping and persistent postoperative pain requiring the administration of nonnarcotic analgesics for 24 hours [das Dores et al., 1999; Perlitz et al., 2001; Römer et Müller, 1999; Römer et al., 2000; Weisberg et al., 2000].

The insulated sheath is inserted into the cervical os under hysteroscopic visualization and kept there throughout the ablation procedure. It follows that the risk of uterine perforation or cervical laceration is lower. The diagnostic hysteroscopy performed prior to treatment enables the physician to check that there are no uterine perforations and to detect any intrauterine pathology not previously diagnosed. Since the procedure is performed with direct visual monitoring, the physician can monitor the insertion of the insulated sheath and observe the destruction of endometrial tissue [Weisberg et al., 2000]. Irrigation of the uterine cavity (including the cornual regions) with heated normal saline destroys benign tumors that are sometimes anchored on the uterine wall [das Dores et al., 1999; Römer et Müller, 1999; Weisberg et al., 2000]. However, it is important to carefully select candidates for this operation, since a large fibroid deforming the uterine cavity would prevent adequate irrigation [das Dores et al., 1999; Richart et al., 1999]. Among the contraindications to hydrothermal endometrial ablation (HTA), particular mention should be made of an active genital or urinary tract infection and any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy [FDA, 2001d]. It should be noted that the cervix has to be dilated to 8 mm in order to insert the device and that the dilatation process can be painful, even with local anesthesia.

5.2.4 Cryoablation

Cahan and Brockunier were the first to describe the treatment of dysfunctional uterine bleeding with endometrial cryoablation. They had treated six women by exposing their endometrium to temperatures ranging from −60 to −100°C [Cahan and Brockunier, 1967]. Four of the women experienced a marked decrease in or normalization of menstrual blood loss, with unchanged or increased menstrual blood loss in the other two. One of the women developed an intrauterine abscess. A second case of intrauterine abscess due to endometrial cryoablation using Cahan and Brockunier's technique was reported in the literature as well [Burke et al., 1973]. Various uterine cryosurgery techniques were described in a series of articles [Droegemueller et al., 1970; Droegemueller et al., 1971a; Droegemueller et al., 1971b; Droegemueller et al., 1978]. Amenorrhea was achieved in close to half the patients up to two months after treatment.

Recently, use was made of a device that yields constant, low (−45°C) temperatures by means of a gas (nitrous oxide) to treat dysfunctional uterine bleeding in 67 women [Pittrof et al., 1994]. None of the women who were treated became amenorrheic, but 63% of them experienced reduced menstrual flow up to 18 months after the procedure. Kumar et al. evaluated a similar technique, which they used to treat dysfunctional uterine bleeding in 27 women [Kumar et al., 2002]. Three months after endometrial cryoablation, the amenorrhea rate was 7.4%, 63.0% of the women were experiencing markedly reduced or normalized menstrual blood loss, and 29.6% of them had unchanged or increased menstrual flow. A third clinical study evaluated the efficacy of a similar device, but one which can maintain the temperature at −120°C using liquefied gas (nitrogen), in 15 women. The amenorrhea rate was 75.5% six months after cryosurgery and 50.3% after 22 months of follow-up [Rutherford et al., 1998].

However, certain factors are preventing broader use of the existing cryosurgery devices for endometrial ablation. To start with, their operating principle is the circulation of liquid nitrogen in a cryoprobe or the expansion of a gas (Joule-Thompson effect[8]), such as nitrous oxide or argon. The liquid nitrogen-based devices produce very low temperatures (−120 to −140°C) and are bulky and expensive. Those that use nitrous oxide and produce low temperatures (−50 to −60°C) are generally smaller and less expensive. However, the temperatures achieved are not low enough, and the operating pressure is high (5,172 kPa). The operating pressure of the argon-based devices, which produce very low temperatures (−120°C), is far too high (20,690 kPa). In fact, such a high operating pressure raises concerns about these devices' safety [Dobak et al., 2000a].

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[8] The cooling occurring when a compressed gas expands without producing any work.

The Her Option™ and Soprano™ cryotherapy systems have been specifically designed for endometrial ablation in the treatment of dysfunctional uterine bleeding. The destruction of the endometrium and superficial myometrium with these devices is based on local freezing. However, the cervix has to be dilated to 6 mm in order to insert the cryoprobe up to the uterine fundus. Hysterosonography is performed to check that the probe is properly positioned in the uterine cavity and to monitor the growth of the iceball during the treatment cycles.

The efficacy and safety of the Soprano Cryotherapy System have not been established in published randomized, controlled trials. Furthermore, a search in the computerized literature databases did not yield any published uncontrolled clinical studies. This system is briefly described in appendix B. As at July 31, 2002, it had not been approved by the HPFB.

5.2.4.1 Her Option™ Uterine Cryoblation Therapy™ System

The operation of the Her Option (previously First Option™) System is based on the Joule-Thompson effect. A cryoprobe is connected to a compressor by flexible tubing. It is controlled by a single-use, sterile unit (5.5 mm in diameter) whose metal tip fits over the freezing tip of the cryoprobe [Dobak and Willems, 2000; Dobak et al., 2000a; Dobak et al., 2000b]. Gas diffuses through a small orifice and cools as its pressure changes. An iceball forms when the temperature of the cryoprobe tip is between −100 and −120°C [FDA, 2001b]. The device causes necrosis to a depth of 6 to 12 mm [Dobak and Willems, 2000; Dobak et al., 2000a; Dobak et al., 2000b]. The first treatment cycle takes four minutes [Dobak and Willems, 2000; Dobak et al., 2000b]. Depending on the characteristics of the uterus, one to three additional treatment cycles of 6 minutes' duration may be necessary to properly treat the entire target area [Dobak and Willems, 2000; Dobak et al., 2000b; Sanders, 2001].

A search in the computerized literature databases did not yield any published uncontrolled clinical studies of the efficacy and safety of endometrial cryoablation (Her Option) in the treatment of dysfunctional uterine bleeding. A randomized, multicentre trial comparing endometrial cryoablation (Her Option) and rollerball ablation was conducted after the successful completion of preclinical studies and a study of ablation just before hysterectomy [Dobak and Willems, 2000; Dobak et al., 2000a; Dobak et al., 2000b]. The results of this clinical trial were published and are presented later in this report.

Since endometrial cryoablation does not require uterine distension, this technique can be used for submucous fibroids [Dobak et al., 2000b]. Uterine leiomyomas do not seem to affect iceball growth and are easily destroyed by freezing [Dobak and Willems, 2000]. Hysterosonography is performed to check that the cryoprobe is properly positioned and to monitor the freezing [Dobak and Willems, 2000]. Endometrial cryoablation (Her Option) is specifically contraindicated in the presence of an active genital or urinary tract infection or any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy [FDA, 2001b].

5.2.5 Impedance-controlled ablation

5.2.5.1 NovaSure™ Impedance Controlled Endometrial Ablation System

The NovaSure's radiofrequency controller is connected to a single-use device consisting of a 7-mm-diameter, rigid tube housing a metallic mesh triangular electrode. The cervix has to be dilated to 8 mm in order to insert the tube up to the uterine fundus [FDA, 2001f]. The triangular electrode is then expanded out of the tube into the uterine cavity. Suction created by the controller brings the uterine mucosa in close contact with the electrode before ablation begins [Cooper and Erickson, 2000; FDA, 2001f]. Radiofrequency energy desiccates and coagulates the endometrium and the underlying superficial myometrium. As tissue destruction progresses, electrical impedance of the tissues increases [FDA, 2001f]. The procedure terminates automatically when impedance at the tissue-electrode interface reaches the preset cutoff of 50 ohms, tissue destruction having reached a sufficient depth, or when the total treatment time reaches 120 seconds. The treatment takes 40 to 120 seconds (90 seconds on average), depending on the thickness of the endometrial tissue [Cooper and Erickson, 2000; FDA, 2001f].

A search in the computerized literature databases did not yield any published uncontrolled clinical studies of the efficacy and safety of impedance-controlled endometrial ablation (NovaSure) in the treatment of dysfunctional uterine bleeding. A randomized, multicentre trial comparing this technique (NovaSure) and transcervical resection was conducted after the successful completion of preclinical and clinical studies (prehysterectomy studies and feasibility studies) [FDA, 2001f]. The results of this clinical trial were published and are presented later in this report.

It should be noted that the documentation provided by the manufacturer very briefly presents the results of two randomized trials that compared impedance-controlled ablation (NovaSure) and thermal balloon ablation (ThermaChoice and Cavaterm) and the results of a clinical study conducted in Europe[9]. Despite a search in the computerized literature databases, we did not find any published report of these results when this report was being drafted. Given the paucity of published data, these three clinical studies were not included in this assessment.

Impedance-controlled ablation does not require pretreatment with endometrial thinning agents. This technique can be performed at any time during the menstrual cycle, even during menstruation [Cooper and Erickson, 2000]. The device includes a uterine cavity integrity assessment system designed to reduce the risk of complications, such as perforation. The minimum length of the electrode array is 4 cm. Thus, treating a uterine cavity less than 4 cm in length could cause thermal injury to the endocervical canal [FDA, 2001f]. Among the contraindications to impedance-controlled endometrial ablation (NovaSure), particular mention should be made of an active genital or urinary tract infection or any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy [FDA, 2001f]. It should be noted that the cervix has to be dilated to 8 mm in order to insert the device and that the dilatation process can be painful, even with local anesthesia.

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[9] Written communication from E. Skalnyi, M.D., Scientific Director, Novacept, United States, May 2001.

5.3 Comparison of surgical treatments

5.3.1 Comparison of endometrial ablation techniques and hysterectomy

The results of a meta-analysis of randomized, controlled trials and two case-control studies had been published when this report was drafted. The results in question are presented in detail in Appendix D.

In a systematic review, endometrial ablation techniques were compared with hysterectomy in the treatment of uterine bleeding [Lethaby et al., 2000d]. The authors selected papers from five randomized, controlled trials that met the inclusion criteria for the review [Crosignani et al., 1997a; Dwyer et al., 1993; Gannon et al., 1991; O'Connor et al., 1997; Pinion et al., 1994], plus a certain number of papers containing the results of the trials conducted by Dwyer et al. and Pinion et al. [Grant et al., 1999; Sculpher et al., 1993; Sculpher et al., 1996]. The authors of these articles assess the different treatment outcomes for different follow-up time points in the same patients. In four of the five clinical trials selected, the procedure performed was transcervical resection [Crosignani et al., 1997a; Dwyer et al., 1993; Gannon et al., 1991; O'Connor et al., 1997]. In the fifth trial, as many transcervical resections were performed as laser ablations, but the trial did not have the necessary statistical power to compare these two techniques [Pinion et al., 1994]. All of the endometrial ablation techniques were therefore lumped together for the purposes of the systematic review.

Four clinical trials evaluated quality of life after the procedure, but the evaluation was done using different methods. Thus, the systematic review concerned quality of life as measured by the Golombok Rust Inventory of Marital State (one year after the operation), the Short Form 36 (SF-36) scale, the Euroqol visual analog scale, the Hospital Anxiety and Depression Scale (HAD) and the Sabbatsberg Sexual Rating Scale (two years after the operation). The SF-36 health survey questionnaire provides a global, subjective assessment of eight multi-item dimensions, namely, limitations on work or social activities because of health problems, limitations on social activities because of physical or emotional problems, limitations on physical functional capacity and usual role activities because of physical or emotional problems, mental health, vitality, pain, and the patient's general health perceptions. The Euroqol provides a global assessment, expressed as a single index figure, of quality of life in terms of health. The researchers modified the Golombok Rust Inventory of Marital State in order to measure the overall quality of marital relations, whereas the patients used the Sabbatsberg Sexual Rating Scale to assess the quality of their sexual relations on their own. Lastly, the Hospital Anxiety and Depression Scale is a mood self-assessment instrument concerning anxiety and depression. The results of the meta-analysis are presented in Table D.1.

The systematic review showed that endometrial ablation techniques are considerably superior to hysterectomy in terms of immediate benefits. Thus, endometrial ablation takes significantly less time, results in a shorter hospital stay and permits a significantly speedier return to work than hysterectomy. However, the assessments based on the analysis are not reliable and should be viewed with caution because of considerable study design differences. We therefore do not know if these differences are of substantial clinical significance.

Prior to discharge from hospital, the women who had been treated by hysterectomy were exposed to a greater risk of septicemia, blood transfusion, urinary retention, anemia, pyrexia, surgical wound hematoma, vaginal vault hematoma, and cautery for hypergranulation. No differences were observed between the two groups in terms of the risk of hemorrhage, perforation, gastrointestinal obstruction or laparotomy for a postoperative complication.

Failure of the initial operation required reintervention in a larger proportion of women who had undergone endometrial ablation. All of the odds ratios were highly significant. They ranged from 4.45 to 9.84, depending on the duration of the follow-up after the first operation.

At the end of this systematic review, the authors conclude that there was a significant advantage in favour of hysterectomy in relation to endometrial ablation. First, it invariably led to amenorrhea, while endometrial ablation ended in failure one year after the first operation in 3 to 13% of the women.

Second, after the first year of follow-up, hysterectomy led to an improvement in general health in a larger proportion of the women than did endometrial ablation. After four years of follow-up, the difference between the two groups had diminished and was slightly above the 0.05 significance threshold. However, no marked difference was noted between the two procedures with regard to the measurement of quality of life. On the other hand, significant differences were observed for three dimensions in the SF-36 questionnaire, which the participants answered two years after their operation. The scores for the ability to engage in social activities, for pain and for general health perceptions were in favour of hysterectomy.

Lastly, the level of satisfaction (very and moderately satisfied) two years after the first operation was considerably higher in the women treated by hysterectomy than those treated by endometrial ablation.

In a first retrospective, single-centre case-control study, the clinical outcomes obtained in menorrhagic women treated by rollerball ablation or hysterectomy (all approaches combined) were compared [Hidlebaugh and Orr, 1998]. The mean duration of follow-up was 48.5 months in the rollerball ablation group and 36 months in the hysterectomy group (see Table D.2).

Based on the results of this study, rollerball ablation is more advantageous than hysterectomy in certain respects. It takes significantly less time, results in a shorter hospital stay and permits a significantly speedier return to the activities of daily living than hysterectomy.

The total incidence of complications was 7.8% and 34.8% in the rollerball ablation group and the hysterectomy group, respectively. The intraoperative and postoperative complications of rollerball ablation were uterine perforation, in one case, fluid overload, in two cases, and endometritis, in two other cases. This technique did not cause any late complications requiring rehospitalization. The intraoperative and postoperative complications of hysterectomy included hemorrhage (one case), bladder injury (one case), fever (six cases), urinary tract infection (two cases), intestinal obstruction (one case) and surgical wound hematoma (one case). Four women had to be rehospitalized because of late complications, such as vaginal cellulitis, pelvic abscess, vaginal vault hemorrhage, and obstruction of the small intestine.

A repeat ablation was required in 2 (3.1%) of the women treated by rollerball ablation, and 6 (9.4%) of the women had to undergo a hysterectomy because of an insufficient reduction in menstrual blood loss. Five of the women treated by hysterectomy were readmitted to the gynecology or surgical ward on a total of seven occasions during the three years following the initial surgery.

All the women became amenorrheic after hysterectomy, while endometrial ablation ended in failure in about 13% of the women who had undergone this procedure. More than 8 women in 10 treated by endometrial ablation indicated that they were satisfied with the treatment outcome. Unfortunately, the authors did not determine the satisfaction rate in the patients treated by hysterectomy.

The results of a second case-control study were recently published [Mousa et al., 2001]. This retrospective, single-centre study compared the medium-term clinical outcomes in menorrhagic women treated by rollerball ablation versus abdominal hysterectomy (with preservation of at least one ovary). The mean time that had elapsed from the initial operation was 32 months (range: 18 to 55 months). The results of this retrospective study are presented in Table D.3.

This study, too, shows that rollerball ablation is superior to abdominal hysterectomy in certain respects, such as the length of hospital stay, which was much shorter. Furthermore, the time taken to return to normal daily activities was only two weeks in most of the women treated by rollerball ablation and eight weeks in slightly more than half of those treated by hysterectomy.

The total incidence of complications was 5.1% and 12.5% in the ablation group and hysterectomy group, respectively. In the rollerball-treated women, four intraoperative complications occurred, namely, two cases of uterine perforation, one case of hemorrhage and one of fluid overload. No serious complications occurred during the abdominal hysterectomies. However, the postoperative complications included two cases of wound infection, one case of surgical wound hematoma and two of urinary tract infection.

Additional treatment had to be administered to 10 of the women (12.5%) treated by rollerball ablation, because of insufficient relief of symptoms. Three women responded to medical treatment and did not require further intervention. An abdominal hysterectomy was performed in one woman after failed medical treatment and in six others who had not received any type of adjuvant medical treatment. Lastly, other surgical interventions had to be performed or other diagnoses made in 6 of the 40 women (15.0%) initially treated by abdominal hysterectomy.

All the women treated by hysterectomy became amenorrheic, whereas menstrual blood loss was unchanged in 7.5% of the women treated by rollerball ablation. Hysterectomy provided symptomatic relief in a greater proportion of women than rollerball ablation. In fact, the authors observed a significant difference in terms of premenstrual syndrome relief and the incidence of dysmenorrhea.

Abdominal hysterectomy yielded a considerably higher satisfaction rate than rollerball ablation. Most of the subjects in both groups reported an improvement in their lifestyle after the operation. In fact, rollerball ablation led to an improvement in sexual functioning in a greater proportion of women than hysterectomy. On the other hand, the ability to perform housework and the ability to work improved in 100% of the women treated by hysterectomy, for both items, and in 84.6% and 90.3%, respectively, of the women treated by rollerball ablation. However, these differences were not statistically significant.

As in the case of the meta-analysis [Lethaby et al., 2000d], the results of both case-control studies of rollerball endometrial ablation and hysterectomy indicate that rollerball ablation requires less time and results in a considerably shorter hospital stay and convalescence than hysterectomy. Hysterectomy offers the advantage of guaranteeing amenorrhea and yielding a higher satisfaction rate, but it exposes women to a greater risk of postoperative and late complications.

5.3.2 Comparison of endometrial ablation techniques

Controlled studies of the various endometrial ablation techniques are few in number. They are summarized in Appendix E. Only the results of five randomized, controlled trials and of one large, nationwide, prospective survey that had been published when this report was being drafted are presented in this section. The results of a nonrandomized, controlled, prospective study and of two case-control studies are presented in Appendix F.

5.3.2.1 Comparison of laser ablation and the other first-generation ablation techniques

Laser ablation and transcervical resection (together with treatment of the uterine fundus and cornual regions with a rollerball electrode) were compared in a single, 12-month, randomized trial [Bhattacharya et al., 37]. In all, 185 laser ablations and 181 transcervical resections were performed.

The main outcome measures were intraoperative complications, time to recovery, the effects on menstruation, the need for surgical reintervention, patient satisfaction and resource utilization. Menstrual blood loss was evaluated by means of a clinical questionnaire. The participants were asked to record the degree of uterine bleeding and dysmenorrhea on a 5-point scale each day of their periods. A total result was obtained by combining these results. Lastly, the psychological effects were measured on the HAD scale (see Table 2).

It was found that transcervical resection required significantly less time to perform and resulted in significantly less theatre time than laser ablation. The authors did not observe any difference between these two techniques in terms of the median length of hospital stay.

There were three cases of uterine perforation in the transcervical resection group. During the tubal ligation performed at the same time as the endometrial ablation, sustained thermal injury to the cornual regions was detected in two laser-treated women. Obstruction of the small intestine resulted in the rehospitalization of another laser-treated woman, as well as a laparotomy and a bowel resection. This woman, who was the only participant in this trial to experience a major complication, also required a blood transfusion. The postoperative complications included urinary tract infection, pelvic infection and one pregnancy in each group. Two cases of hematometra occurred in the transcervical resection group. Four subjects in each group had to be rehospitalized during the two weeks following the initial operation.

The difference between the two groups with regard to the reintervention rate was not significant. However, transcervical resection resulted in failure requiring hysterectomy more often than did laser ablation (difference: −8.9%; 95% CI: −15 to −3).

As regards the treatment outcomes, the authors observed no marked difference between laser ablation and transcervical resection one year after the initial intervention. Amenorrhea or markedly reduced or normalized menstrual blood loss (hypomenorrhea or eumenorrhea) was achieved in comparable proportions in both groups. Dysmenorrhea was considered to have been reduced, regardless of the surgical technique used. The authors did not observe a significant difference between the two ablation techniques in terms of the incidence of premenstrual symptoms, such as breast tenderness, bloating, irritability, headaches and depression, before or after the operation.

Table 2

Results of a randomized trial that compared laser endometrial ablation and transcervical resection of the endometrium

Outcome measures	Laser ablation	Transcervical resection[a]	95% CI[b]	*P*[c]
PATIENT FLOW (n)				
Subjects randomized	n = 188	n = 184		
Treatment not initiated	3	3		
12 months after the initial intervention				
Reintervention	30	36		
OPERATIVE DATA	n = 185	n = 181		
Operating time (minutes)[d]	30 (± 10.5)	21 (± 7.2)	7.1 to 10.9	< 0.001
Theatre time (minutes)[d,e]	40 (± 11.3)	30 (± 8.7)	7.6 to 12.4	< 0.001
Length of hospital stay (days)[f]	2 (1 to 3)	2 (1 to 3)	–	–
COMPLICATIONS (%)	n = 185	n = 181		
Intraoperative complications				
Uterine perforation[g]	0	1.7	No data	No data
Fluid overload[h]	8.1	1.7	2 to 12	< 0.05
Hemorrhage	3.8	3.3	– 5 to 6	> 0.5
Thermal injury	1.1	0	No data	No data
Technical malfunction	9.2	1.7	3 to 12	< 0.002
Operation aborted	6.5	4.4	–3 to 7	> 0.2
Postoperative complications				
Intestinal obstruction	0.5	0	No data	No data
Urinary tract infection	2.2	1.1	No data	No data
Pelvic infection	2.7	3.3	No data	No data
Pregnancy	0.5	0.5	No data	No data
Hematometra	0	1.1	No data	No data

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[b] 95% confidence interval for the difference; for the continuous variables only.

[c] For the continuous variables, the *P* values are approximations and were calculated manually by the main author of this report from the 95% confidence interval for the difference.

[d] Mean value (± standard deviation [SD]).

[e] Includes the additional time required for sterilization by tubal ligation.

[f] Median value (range).

[g] Includes cervical laceration.

[h] Fluid absorption ≥ 1.5 L.

Source: [Bhattacharya et al., 1997]

Table 2 (Cont'd)

Outcome measures	Laser ablation	Transcervical resection [a]	95% CI [b]	P [c]
COMPLICATIONS (CONT'D)				
Readmissions	2.2	2.2	–	–
Need for surgical reintervention	n = 188	n = 184		
Repeat ablation	11.2	6.0	No data	No data
Hysterectomy	4.8	13.6	–15 to –3	< 0.005
Total	16.0	19.6	–11 to 4	> 0.2
TREATMENT OUTCOMES 12 MONTHS AFTER THE INITIAL INTERVENTION	n = 166	n = 155		
Patient satisfaction				0.8
Very satisfied	68.7	65.8		
Moderately satisfied	20.5	24.5		
Somewhat or not very satisfied	10.2	9.0		
Effect on symptoms				0.6
Cure	24.1	18.1		
Acceptable reduction	41.6	45.8		
Insufficient reduction	22.9	25.2		
No reduction or worsening	10.2	9.7		
Overall health				0.09
Excellent, very good or good	89.8	87.1		
Average or poor	9.0	11.6		
Change in menstrual blood loss	n = 160	n = 146		No data
Amenorrhea	23.1	21.9		
Lighter	49.4	46.6		
Same or heavier	5.6	4.8		
Dysmenorrhea	n = 114	n = 104		No data
None or less	78.1	77.9		
Same or worse	21.9	22.1		

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[b] 95% confidence interval for the difference; for the continuous variables only.

[c] For the continuous variables, the *P* values are approximations and were calculated manually. by the main author of this report from the 95% confidence interval for the difference.

Source: [Bhattacharya et al., 1997]

A comparable proportion of the women in both groups indicated that they were satisfied with the treatment outcomes, that they felt they had been cured or that they had noticed an acceptable reduction in their symptoms. Most of the women treated considered their general health to be good or excellent. A comparison of the changes evaluated by means of the HAD indicated that both techniques yielded similar outcomes. In general, the depression and anxiety scores improved significantly in both groups ($P < 0.001$).

A case-control study with a 4-year follow-up compared laser ablation with transcervical resection and rollerball ablation [Phillips, 1994]. No significant difference was observed between laser ablation and the two electrosurgical techniques in terms of operating time, the mean volume of irrigation fluid absorption, the length of hospital stay or the complication rate (see Table F.1).

Benign pulmonary edema occurred in one woman who had absorbed 4.3 L of irrigation fluid during a laser ablation. Another woman absorbed more than 2.6 L of 1.5% glycine during a transcervical resection. She had no other symptoms apart from postoperative hyponatremia. A single case of uterine perforation occurred during a laser ablation. No cases of intraoperative hemorrhage, postoperative infection, hematometra or cervical stenosis were noted.

The number of repeat ablations following laser ablation and transcervical resection was comparable. During the four years following the initial operation, hysterectomy was required in only one woman (2.1%) treated by laser and in another (11.1%) treated by rollerball.

The treatment outcomes were comparable in the three groups six months and four years after the initial operation. Amenorrhea occurred in a comparable percentage of women in all three groups six months after the initial operation. Four years after the initial surgery, the outcomes were still satisfactory in similar proportions in all three groups.

5.3.2.2 Comparison of rollerball ablation and transcervical resection

Only one randomized, controlled trial, of 5 years' duration, has examined rollerball endometrial ablation and transcervical resection of the endometrium (together with treatment of the uterine fundus and cornual regions with a rollerball electrode) [Boujida et al., 2002]. In all, 120 women were treated, 61 by rollerball ablation and 59 by transcervical resection.

The primary endpoint was the hysterectomy rate during the five years of posttreatment observation. The secondary outcome measures were complications, the decrease in uterine bleeding, patient satisfaction and acceptability of the treatment. The evaluation of uterine bleeding was expressed as a uterine bleeding index. The index was the duration, expressed in days, of uterine bleeding over a 3-month period (see Table 3).

The median duration of rollerball ablation was significantly shorter than that of transcervical resection. One uterine perforation occurred just before an initial ablation and another during a repeat ablation (the authors do not specify the technique). No intraoperative hemorrhage or fluid absorption of 1.5 L or more occurred. However, one patient died from an infection three days after the resection of a uterine fibroid and rollerball endometrial ablation. In all, nine and six cases of postoperative infection were noted in the rollerball ablation group and transcervical resection group, respectively ($P < 0.05$).

Surgical reintervention was required in 20 and 16 women (32.8% and 27.1%), respectively, treated by rollerball ablation and transcervical resection during the five years following the initial surgery. The reintervention consisted of a hysterectomy in 10 of the women (16.4%) treated by rollerball ablation and in 8 (13.6%) of those who had undergone transcervical resection. The difference between the two groups in terms of the number of hysterectomies performed was not significant. The median age (upon study entry) of the women who required a repeat ablation or a hysterectomy was 41.3 years, and that of the women who did not require reintervention was 44.0 years ($P < 0.05$).

Table 3

Results of a randomized trial that compared rollerball endometrial ablation and transcervical resection of the endometrium

Outcome measures	Rollerball ablation	Transcervical resection[a]	*P*
PATIENT FLOW (n)			
Subjects randomized	n = 61	n = 59	
24 months after the initial intervention			
Reintervention	15	14	
Lost to follow-up[b]	5	6	
60 months after the initial intervention			
Reintervention	20	16	
Lost to follow-up[b]	4	3	
OPERATIVE DATA	n = 61	n = 59	
Operating time (minutes)[c]	13	20	< 0.05
General anesthesia (%)	100	100	–
COMPLICATIONS (%)	n = 61	n = 59	
Intraoperative complications			
Uterine perforation[d]	Not specified[e]	Not specified[e]	
Fluid overload[f]	0	0	–
Hemorrhage	0	0	–
Postoperative complications			
Infection	14.8[g]	10.2	> 0.05
Need for surgical reintervention			
24 months after the initial operation			
Repeat ablation	14.8	16.9	No data
Hysterectomy	9.8	6.8	> 0.05
60 months after the initial operation			
Repeat ablation	16.4	13.6	No data
Hysterectomy	16.4	13.6	> 0.05

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[b] Including two patients who died within 24 months following the operation. One, who had undergone rollerball ablation, died following an intraoperative complication, the other of causes unrelated to the intervention (the authors do not indicate which group this patient was in).

[c] Median value.

[d] Includes cervical laceration.

[e] The authors report the occurrence of a uterine perforation right before an initial ablation and of another upon a repeat ablation but do not specify in which group these intraoperative complications occurred.

[f] Fluid absorption ≥ 1.5 L.

[g] Includes one case of serious infection (resulting in death due to disseminated intravascular coagulation three days after the operation).

Source: [Boujida et al., 2002]

Table 3 (Cont'd)

Outcome measures	Rollerball ablation	Transcervical resection[a]	*P*
RESULTS BEFORE THE INITIAL OPERATION	n = 61	n = 59	
Uterine bleeding index[h,i]	36 {33 and 46}	34 {29 and 40}	> 0.05
TREATMENT OUTCOMES 24 MONTHS AFTER THE INITIAL OPERATION	n = 56	n = 53	
Uterine bleeding index[i,j]	13 {10 and 17}	13 {10 and 13}	> 0.05
TREATMENT OUTCOMES 60 MONTHS AFTER THE INITIAL OPERATION	n = 57	n = 56	
Uterine bleeding index[i,k]	16 {12 and 18}	18 {15 and 27}	> 0.05
Satisfaction and acceptability	n = 61	n = 59	
Would recommend the treatment to their best friends	80.3	78.0	> 0.05

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[h] The duration, expressed in days, of uterine bleeding over a 3-month period (including spotting).

[i] Median value {5th and 95th percentiles}.

[j] For the 60 subjects whose bleeding persisted (the authors do not specify the number of subjects per group).

[k] For the 40 subjects whose bleeding persisted (the authors do not specify the number of subjects per group).

Source: [Boujida et al., 2002]

As for the treatment outcomes, no marked difference was observed between rollerball ablation and transcervical resection two and five years after the initial intervention. The median duration of uterine bleeding per 3-month period had decreased by one-half in both groups. Five years after the initial operation, both techniques were still yielding high satisfaction and treatment acceptability rates. Close to 80% of the women treated with either technique would recommend the treatment to their best friends.

5.3.2.3 Comparison of microwave ablation (MEA) and transcervical resection

When this report was being drafted, only one randomized, controlled trial, of 12 months' duration, had examined microwave endometrial ablation (MEA) and transcervical resection of the endometrium (together with rollerball treatment of the uterine fundus and cornual regions) [Cooper et al., 1999a]. In all, 263 women were treated, 129 by microwave ablation and 134 by transcervical resection.

The primary endpoints were patient satisfaction and acceptability of the surgical treatment. The secondary outcome measures were the effects on menstruation, operative data and complications, and quality of life as assessed by means of the SF-36 questionnaire. Menstrual blood loss was evaluated by means of a clinical questionnaire. The participants were asked to record the degree of uterine bleeding and dysmenorrhea on a 5-point scale each day of their periods. A total result was obtained by combining these results (see Table 4).

Despite the fact that carbon dioxide (CO_2) hysteroscopy was performed prior to treatment, the mean operating time for microwave ablation was significantly shorter than for transcervical resection.

Table 4

Results of a randomized, controlled trial and of a medium-term follow-up study of microwave endometrial ablation (MEA) and transcervical resection of the endometrium

Outcome measures	MEA	Transcervical resection[a]	95% CI[b]	P
PATIENT FLOW (n)				
Subjects randomized	n = 129	n = 134		
12 months after the initial intervention				
Reintervention	10	13		
Lost to follow-up	13	10		
24 months after the initial intervention				
Reintervention	16	18		
Lost to follow-up	9	5		
OPERATIVE DATA[c]	n = 129	n = 134		
Operating time (minutes)	11.4 (± 10.5)[d]	15.0 (± 7.2)	−5.7 to 1.4	0.001
Theatre time (minutes)	20.9 (± 11.3)	26.2 (± 8.7)	−7.7 to 2.8	< 0.001
Length of hospital stay (hours)	13.4 (± 17.6)	16.7 (± 21.2)	−8.0 to 1.5	0.17
General anesthesia (%)	100	100	–	–
COMPLICATIONS (%)	n = 129	n = 134		
Intraoperative complications				
Uterine perforation[e]	0.8	0.7	No data	–
Fluid overload[f]	0	0.7	No data	–
Hemorrhage	0	3.7	0 to 7	0.06
Technical malfunction	8.5	2.2	1 to 12	0.02
Operation aborted	3.9	3.7	−4 to 5	0.57
Postoperative analgesia				
None	69.8	73.9	−15 to 7	0.48
Oral	17.8	14.2	No data	–
Injection	10.9	11.9	No data	–
Postoperative complications[g]				
Pregnancy	0.8[h]	0	No data	–
Need for surgical reintervention				
12 months after the initial operation				
Repeat ablation	0.8	1.5	No data	–
Hysterectomy	7.0	9.0	No data	–
24 months after the initial operation				
Repeat ablation	0.8	1.5	No data	–
Hysterectomy	11.6	12.7	No data	–

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[b] 95% confidence interval for the difference.

[c] Mean (± SD).

[d] Includes diagnostic CO_2 hysteroscopy performed before the start of treatment.

[e] Includes cervical laceration.

[f] Fluid absorption ≥ 1.5 L.

[g] No postoperative complications reported during the 12 months following the initial intervention.

[h] Occurred 17 months after the initial operation.

Source: [Cooper et al., 1999a; Bain et al., 2002]

Table 4 (Cont'd)

Outcome measures	MEA	Transcervical resection[a]	95% CI[b]	*P*
TREATMENT OUTCOMES 12 MONTHS AFTER THE INITIAL INTERVENTION	n = 116	n = 124		
Menstruation and symptoms (%)				
Amenorrhea	39.7	39.5	–14 to 20	0.23
Blood loss same or heavier	7.8	8.9	–19 to 26	0.98
Dysmenorrhea same or worse	20.7	17.7	–11 to 20	0.62
No work absenteeism due to menstruation	82.8	81.5	–14 to 18	0.92
Quality of life				
SF-36 questionnaire[c]				
Physical functional capacity	0.7 (± 18.9)	2.4 (± 16.8)	–6.4 to 2.9	0.58
Limitations on social activity	20.6 (± 26.5)	16.2 (± 24.4)	–2.1 to 10.9	0.12
Limitations due to physical problems	23.9 (± 49.4)	11.3 (± 41.7)	1.0 to 24.3	0.03
Limitations due to emotional problems	17.0 (± 48.5)	13.7 (± 47.9)	–9.1 to 15.6	0.38
Mental health	6.3 (± 19.5)	6.0 (± 22.2)	–4.9 to 5.7	0.83
Vitality	12.8 (± 21.7)	12.1 (± 23.0)	–4.9 to 6.5	0.58
Pain	14.8 (± 31.0)	7.2 (± 31.1)	–0.2 to 15.5	0.54
General health	2.4 (± 20.3)	2.9 (± 20.0)	0.2 to 10.5	0.06
Satisfaction and acceptability (%)				
Completely or generally satisfied	76.7	75.0	–12 to 17	0.88
Surgical treatment acceptable	94.0	90.3	–11 to 35	0.34
Would recommend the treatment to other women	90.5	88.7	–16 to 25	0.68
TREATMENT OUTCOMES 24 MONTHS AFTER THE INITIAL INTERVENTION	n = 120	n = 129		
Menstruation and symptoms (%)				
Amenorrhea	47.5	41.1	–9 to 15	0.19
Blood loss same or heavier	6.7	10.9	–11 to 3	0.10
Dysmenorrhea same or worse	18.3	22.5	–14 to 5	0.78
Quality of life				
SF-36 questionnaire[c]				
Physical functional capacity	2.3 (± 21.3)	0.9 (± 20.4)	–3.8 to 6.6	0.28
Limitations on social activity	10.1 (± 27.5)	6.2 (± 23.7)	–2.5 to 10.3	0.33
Limitations due to physical problems	18.5 (± 53.7)	6.1 (± 43.8)	–0.2 to 24.6	0.06
Limitations due to emotional problems	17.8 (± 47.5)	4.2 (± 40.1)	–3.6 to 23.5	0.17
Mental health	6.0 (± 21.6)	4.1 (± 19.8)	–3.3 to 6.9	0.44
Vitality	11.4 (± 25.1)	11.8 (± 22.6)	–6.4 to 5.5	0.90
Pain	13.5 (± 31.7)	3.0 (± 29.8)	2.9 to 18.2	0.02
General health	0.0 (± 24.4)	–2.9 (± 19.0)	–2.5 to 8.4	0.29
Satisfaction and acceptability (%)				
Completely or generally satisfied	79.0	67.0	7 to 22	0.02
Surgical treatment acceptable	96.0	88.0	0.06 to 14	0.03
Would recommend the treatment to other women	90.0	90.0	–	–

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[b] 95% confidence interval for the difference.

[c] Mean (± SD).

Source: [Cooper et al., 1999a; Bain et al., 2002]

The length of postoperative hospital stay was also slightly shorter after microwave ablation, but the difference between the two techniques was not significant.

One transcervical resection had to be aborted because 1.5 L of glycine had been absorbed. Five cases of intraoperative hemorrhage occurred in the transcervical resection group. One case of uterine perforation occurred in each of the two groups. Technical malfunctions occurred significantly more often with the MEA than with the resectoscope, with four women in the microwave group undergoing transcervical resection because of microwave equipment failure. However, all of these events occurred at the beginning of the study, when a prototype microwave generator was being used.

During the 12 months following the initial operation, further surgery was required in 10 women (7.8%) treated by microwave ablation and 13 women (9.7%) treated by transcervical resection.

Both surgical techniques resulted in a significant reduction in menstrual flow and work absence due to menstrual symptoms ($P < 0.001$), with no difference observed between the two groups. The proportion of women who reported a significant decrease in dysmenorrhea and premenstrual syndrome was comparable in both groups. Based on the changes in the answers to the SF-36 questionnaire, microwave ablation resulted in an improvement in the eight dimensions covered ($P < 0.001$ for six of these dimensions), transcervical resection in seven of them (P values between < 0.05 and < 0.001). Both techniques yielded generally comparable results, although microwave ablation led to a greater improvement in limitations due to physical health problems.

Twelve months after the initial intervention, both techniques were still yielding high satisfaction and treatment acceptability rates. The proportion of women who were completely or generally satisfied with the treatment outcomes was comparable in both groups. Furthermore, most of the women treated found the treatments acceptable and would recommend them to other women.

The results of the 2-year follow-up of the patients treated in the randomized, controlled trial conducted by Cooper et al. [1999a] were recently published [Bain et al., 2002]. In all, 249 women (94.7%) answered questionnaires mailed 24 months after the initial operation.

The pregnancy that occurred in one woman treated by microwave ablation was considered a postoperative complication. She became pregnant 17 months after the initial ablation, and the pregnancy was interrupted at nine weeks. She was amenorrheic at the time of conception and was not using any contraception, despite recommendations. During the 24 months following the initial operation, further surgery was required in 16 women (12.4%) treated by microwave ablation and 18 women (13.4%) treated by transcervical resection.

Two years after the initial intervention, the treatment outcomes were comparable in both groups. Both techniques resulted in a reduction in menstrual flow and dysmenorrhea. Based on changes in the answers to the SF-36 questionnaire, microwave ablation led to an improvement in seven of the dimensions covered (P values between < 0.05 and < 0.001), as did transcervical resection (P values between < 0.05 and < 0.001 for four of these dimensions). Both techniques yielded generally comparable results, although microwave ablation provided greater pain relief. In general, the scores for all of the variables considered did not seem to be affected by the passage of time.

Twenty-four months after the initial operation, the two techniques were still yielding high satisfaction and treatment acceptability rates. However, the proportion of women treated by microwave ablation who were satisfied with the treatment outcomes and who considered the treatments acceptable was higher than that of women treated by transcervical resection ($P = 0.02$ and 0.03, respectively).

5.3.2.4 Comparison of thermal balloon ablation (ThermaChoice) and first-generation ablation techniques

When this report was being drafted, there had been just one randomized, controlled trial, of 12 months' duration, of thermal balloon ablation (ThermaChoice) and rollerball ablation [FDA, 1997; Meyer et al., 1998]. Data on 261 anesthetized women were examined for the purpose of assessing the safety of the treatments. In all, 255 of these women were eventually treated under the protocol, 131 by thermal balloon ablation and 124 by rollerball ablation.

Menstrual blood loss was evaluated prospectively using a validated pictorial chart method [Higham et al., 1990][10]. Treatment success (primary endpoint) was a reduction in scores of at least 150 before treatment to 75 or less one year after the initial operation. The secondary outcome measures were quality of life and satisfaction with the treatment (see Table 5).

Operative time for thermal balloon ablation was significantly shorter than for rollerball ablation, with surgery completed in less than 30 minutes in 71.0% of the women treated by thermal balloon ablation and 28.6% of those treated by rollerball ablation. General anesthesia was used in 53.7% of the women in the thermal balloon group and 84.1% of those in the rollerball group.

No intraoperative complications were noted in the women treated by thermal balloon ablation, but four women (3.2%) in the rollerball group did experience such complications. The postoperative complications noted 12 months after the initial ablation included three cases of endometritis, one of urinary tract infection and one of postcoital bleeding in the thermal balloon group, and one case of endometritis, one of hematometra and one of hydrosalpinx in the rollerball group.

A hysterectomy was required in two (1.5%) and three (2.4%) of the women in the thermal balloon group and rollerball group, respectively, during the 12 months following the initial operation.

The treatment success rates were comparable in both groups. Twelve months after the initial operation, the diary score was 75 or less in 80.2% and 84.3% of the thermal balloon-treated women and the rollerball-treated women, respectively. The amenorrhea rate 12 months after the initial operation was higher in the rollerball group than in the thermal balloon group. The mean diary score had decreased by 85.5% in the thermal balloon group and by 91.7% in the other group ($P < 0.05$). Nonetheless, analysis of variance did not reveal any difference between the two techniques in terms of variability of the mean diary score during the follow-up. As indicated by the pictorial chart scores, there was a tendency toward improvement in both groups throughout the 12 months following the initial intervention.

As determined from quality-of-life questionnaires, the satisfaction rate was high for both techniques 12 months after the initial operation. The proportion of women who were satisfied or very satisfied with the treatment outcomes was similar in both groups. Furthermore, the vast majority of the women in both groups indicated that their menstrual blood loss now had little or no effect on their quality of life.

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[10] See section 2.1.

Table 5

Results of a randomized, controlled trial and of two follow-up studies, one medium-term, the other long-term, of thermal balloon endometrial ablation (ThermaChoice) and rollerball endometrial ablation

Outcome measures	ThermaChoice	Rollerball ablation	*P*
PATIENT FLOW (n)			
Subjects randomized	n = 137	n = 138	
Procedure not initiated	3	12	
Procedure aborted	3	2	
12 months after the initial intervention			
Reintervention	2	3	
Lost to follow-up	4	7	
24 months after the initial intervention			
Reintervention	4	9	
Lost to follow-up	5	10	
36 months after the initial intervention			
Reintervention	9	14	
Lost to follow-up	7	10	
Pregnancy	1	0	
OPERATIVE DATA	n = 134	n = 126	
Operating time (minutes)[a]	27.4 (± 11.8)	39.6 (± 14.7)	< 0.05
General anesthesia (%)	53.7	84.1	< 0.05
COMPLICATIONS (%)			
Intraoperative complications	n = 134	n = 126	No data
Uterine perforation[b]	0	1.6	
Fluid overload[c]	0	1.6	
Technical malfunction	18.7	10.3	
Postoperative complications[d]	n = 134	n = 126	No data
Pelvic cramping	91.8[e]	No data	
Endometritis	2.2	0.8	
Urinary infection	0.7	0	
Hematometra	0	0.8	
Postcoital bleeding	0.7	0	
Hydrosalpinx	0	0.8[f]	
Pregnancy	0.7[g]	0	
Need for surgical reintervention	n = 131	n = 124	
12 months after the initial operation			No data
Repeat ablation	0	0	
Hysterectomy	1.5	2.4	
24 months after the initial operation			No data
Repeat ablation	0	0	
Hysterectomy	3.1	7.3	
36 months after the initial operation			No data
Repeat ablation	0.8	0	
Hysterectomy	6.1	11.3	

[a] Mean (± SD); includes one preoperative curettage of 3 minutes' duration.

[b] Includes cervical laceration.

[c] Fluid absorption ≥ 1.5 L.

[d] Does not include nausea and vomiting.

[e] Mild = 34.3%; moderate = 47.8%; severe = 9.7%.

[f] Occurred one year after the initial operation.

[g] Occurred two and a half years after the initial operation.

Source: [FDA, 1997; Meyer et al., 1998; Grainger et al., 2000; Loffer, 2001]

Table 5 (Cont'd)

Outcome measures	ThermaChoice	Rollerball ablation	*P*
TREATMENT OUTCOMES 12 MONTHS AFTER THE INITIAL INTERVENTION (%)[h]	n = 125	n = 114	
Diary score[i]			
≤ 75[j]	80.2 [73.2 to 87.2]	84.3 [77.6 to 90.9]	> 0.05
≤ 100[k]	84.8	89.5	> 0.05
0[l]	13.2	27.2	< 0.05
Mean reduction[m]	85.5 (± 22.5)	91.7 (± 12.0)	< 0.05
Reduction ≥ 90%	61.6	68.4	> 0.05
Quality of life			
Major effect[n]	70.3/3.2	78.6/1.8	> 0.05
Premenstrual syndrome[n]	91.2/72.8	91.3/71.9	> 0.05
Reduction in dysmenorrhea	70.4	75.4	> 0.05
Work absenteeism due to menstruation[n]	39.7/4.0	41.9/2.7	> 0.05
Patient satisfaction			
Very satisfied	85.6	86.7	> 0.05
Satisfied	10.4	12.4	> 0.05
TREATMENT OUTCOMES 24 MONTHS AFTER THE INITIAL INTERVENTION (%)[h]	n = 122	n = 105	
Menstruation			
Amenorrhea	13.1	21.9	< 0.05
Spotting, hypomenorrhea or eumenorrhea	76.2	68.6	> 0.05
Quality of life			
Major effect	4.9	1.0	> 0.05
Work absenteeism due to menstruation	0.8	2.9	> 0.05
Patient satisfaction			
Very satisfied	86.1	86.7	> 0.05
Satisfied	9.8	11.4	> 0.05
TREATMENT OUTCOMES 36 MONTHS AFTER THE INITIAL INTERVENTION (%)[o]	n = 114	n = 100	
Menstruation			
Amenorrhea	14.9	26.3	< 0.05
Spotting, hypomenorrhea or eumenorrhea	78.1	67.7	> 0.05
Quality of life			
Major effect	1.8	2.0	> 0.05
Work absenteeism due to menstruation	4.5	5.1	> 0.05
Patient satisfaction			
Satisfied or very satisfied	95.6	97.0	> 0.05

[h] Does not include the women who required surgical reintervention.
[i] Menstrual blood loss assessed using pictorial charts.
[j] Primary endpoint [95% CI].
[k] Uterine bleeding normalized or reduced.
[l] Amenorrhea.
[m] Mean percent reduction in diary scores (± SD).
[n] Prior to treatment/12 months after treatment.
[o] Some women did not answer all the questions.
Source: [FDA, 1997; Meyer et al., 1998; Grainger et al., 2000; Loffer, 2001]

The results of the 2-and 3-year follow-ups of the patients treated in the randomized, controlled trial conducted by Meyer et al. [1998] were recently published [Grainger et al., 2000; Loffer, 2001]. At the end of three years, 41 women (16.1%) had withdrawn from the clinical trial [Loffer, 2001].

The pregnancy that occurred in one woman treated by thermal balloon ablation was considered a postoperative complication. She was amenorrheic 12 and 24 months after the initial operation. She stopped using contraception and became pregnant two and a half years after the initial ablation. During the three years following the initial operation, a larger proportion of women in the rollerball group required surgical reintervention than in the thermal balloon group. The higher trend toward hysterectomy observed after one year of follow-up in the rollerball-treated women persisted after two and three years of posttreatment observation.

Although menstrual blood loss was not evaluated two and three years after the initial operation from pictorial chart scores, reasonable assessments based on the clinician's experience and the patient's history yielded comparable results. The amenorrhea rates remained nearly the same in both groups two and three years after the initial intervention. With the exception of amenorrhea, the authors did not observe a statistically significant difference between the two techniques for any of the clinical efficacy criteria during any of the follow-up visits. The patients' satisfaction rate was similar in both groups and was comparable to the rate observed 12 months after the initial operation. Most of the women were satisfied or very satisfied with the treatment three years after the initial operation. In general, the scores for all of the variables considered did not seem to be affected by the passage of time.

The overall surgical success rate, that is, the percentage of women whose uterine bleeding had become normal or lighter than normal and who did not require surgical reintervention during the three years following the initial operation, was 86.2% (106/123) in the thermal balloon group and 82.3% (93/113) in the rollerball group. These rates were clinically comparable and did not differ significantly from a statistical standpoint.

In a nonrandomized, prospective study with a 24-month follow-up after the initial operation, thermal balloon endometrial ablation (ThermaChoice) was compared with transcervical resection (together with treatment of the uterine fundus and cornual regions with a rollerball electrode) in women with medically refractory menorrhagia [Bongers et al., 2000]. The results of the study are presented in Table F.2.

In the transcervical resection group, this procedure had to be aborted in 13 women, uterine distention having failed in nine cases and technical problems having occurred in the other four. One patient required a hysterectomy the day after the initial operation because of hemorrhage due to a perforation. Three women absorbed more than 2 L of irrigation fluid. In the women treated by thermal balloon ablation, the fluid in the balloon did not reach the required temperature in four cases or the sufficient pressure in four others. In these eight cases, transcervical resection had to be performed instead. No complications were observed after thermal balloon ablation. The number of aborted operations did not differ significantly between the two groups (relative risk [RR]: 1.7; 95% CI: 0.73 to 3.8).

During the two years following the initial intervention, surgical reintervention was required in 9 (11.7%) and 19 (25.3%) of the women treated by thermal balloon ablation and transcervical resection, respectively. Based on a multifactorial statistical analysis, the relative risk of another operation being required was 0.36 [95% CI: 0.05 to 2.5].

The proportion of women who became amenorrheic two years after the initial operation was greater in the transcervical resection group. However, no difference was noted between the two groups in terms of the therapeutic effect or the effect of the passage of time on the number of days during which the women passed blood clots or on the mean duration of menstruation.

A greater proportion of the women in the thermal balloon group indicated they were completely satisfied with the surgical treatment, although the observed difference did not reach the significance threshold. However, significant differences were found in patient satisfaction during the period considered. Patient satisfaction decreased with time (*P* = 0.001), and this decrease was clearly more pronounced in the transcervical resection group than in the thermal balloon group.

A case-control study compared the medium-term clinical outcomes in women treated by thermal balloon ablation (ThermaChoice) or transcervical resection (together with treatment of the uterine fundus and cornual regions with a rollerball electrode) [Gervaise et al., 1999]. None of the women treated had received preoperative hormone therapy for endometrial thinning or undergone vacuum uterine curettage prior to the ablation. In addition, the interventions were not scheduled to be performed at a specific time during the menstrual cycle. The median duration of follow-up was 18.3 months in the thermal balloon group and 19.2 months in the other group (see Table F.3).

Procedure time for thermal balloon ablation was significantly shorter than for transcervical resection, with surgery completed in less than 30 minutes in all the women treated by thermal balloon ablation and in slightly more than half of those who underwent transcervical resection.

No intraoperative complications occurred in either group. Two cases of endometritis that responded to oral antibiotic therapy occurred after transcervical resection, and one woman became pregnant 18 months after thermal balloon ablation. After thermal balloon ablation, four women received progestational hormones and seven (9.6%) had to undergo a hysterectomy. Similarly, progestins were administered to seven women treated by transcervical resection, a repeat resection was performed in one woman (1.3%), and a hysterectomy was performed in five others (6.8%).

The treatment outcomes were comparable in all the study participants. However, the eumenorrhea rate was significantly higher in the thermal balloon group. The treatment outcomes observed 24 months after the initial operation were similar, as well, except with respect to the eumenorrhea rate, which seemed, once again, to be higher in the women who had undergone thermal balloon ablation. However, this difference was not significant. The authors do not mention the effects of the treatment on dysmenorrhea, despite the fact that they constituted a secondary efficacy criterion.

A multivariate statistical analysis showed that the only factor associated with transcervical resection failure was age under 43 years (OR: 3.89; 95% CI: 1.16 to 13.15) and that retroverted uterus was the only factor associated with failure of thermal balloon ablation (OR: 6.2; 95% CI: 1.8 to 21.4). A comparison of the two techniques did not reveal any significant difference in terms of the surgical success rate (based on the cumulative raw frequency of recurrence or treatment failure). Twenty-four months after the initial surgery, the rate was 83.0 ± 5% and 81.1 ± 5% for thermal balloon ablation and transcervical resection, respectively. At the end of the 36-month posttreatment follow-up, these figures were 83.0 ± 5% and 76.3 ± 6%, respectively.

5.3.2.5 Comparison of hydrothermal ablation (HTA) and rollerball ablation

When this report was being drafted, the results of a single randomized, controlled trial, of 12 months' duration, of hydrothermal endometrial ablation (HTA) and rollerball ablation had beenpublished [Corson, 2001; FDA, 2001d]. In all, 276 subjects were randomized. The data on 269 women who had been anesthetized were examined for the purpose of assessing the safety of the treatments. In all, 262 of these women were eventually treated under the protocol, 177 by hydrothermal ablation and 85 by rollerball ablation.

Menstrual blood loss was evaluated prospectively using a validated pictorial chart method [Janssen et al., 1995][11]. Treatment success (primary endpoint) was a reduction in scores of at least 150 before treatment to 75 or less one year after the initial intervention. The secondary outcome measure was quality of life, as assessed by a questionnaire [Ruta et al., 1995]. The questionnaire concerned the duration and regularity of menstrual blood loss, the interval between periods, the degree of bleeding, the number of sanitary napkins or tampons used, spotting, the effect of menstruation on work, leisure activities and sexual functioning, and the need to stay in bed (see Table 6).

It should be noted that there are differences between the safety and efficacy summary prepared by the FDA and the scientific article published by Corson [Corson, 2001; FDA, 2001d]. This situation is all the more curious because the FDA reports the results of Corson's randomized, controlled trial. The results should therefore be the same. However, the difference between the results is especially obvious when it comes to intraoperative complications. For the purposes of this research report and in order to permit a fair comparison of the second-generation ablation techniques, only those surgical complications mentioned in the FDA report are included in Table 6 and mentioned in this section.

Procedure time for the two techniques was comparable. General anesthesia was administered to 55% of the HTA subjects and 76% of the rollerball subjects.

Hydrothermal ablation had to be aborted in seven cases. Technical malfunctions occurred more often with the HTA than with the rollerball resectoscope, with three women undergoing rollerball ablation instead. Cervical laceration (including one case reported only two weeks after the initial operation) occurred in three HTA subjects and two rollerball subjects. Actually, the only serious complication observed in this clinical trial was a cervical laceration that occurred during a rollerball ablation. The day after the operation, the woman in question had a fever, diarrhea, nausea and vomiting. She was readmitted, and laboratory tests revealed gram-negative bacterial septicemia. She responded to antibiotic therapy and was discharged six days later.

The mean duration of postoperative pain was 1.5 ± 1.7 days in the HTA group and 1.4 ± 1.7 days in the rollerball group ($P > 0.05$). The proportion of women who complained of abdominal cramping was higher in the group treated by hydrothermal ablation than in the group treated by rollerball ablation for the entire duration of the follow-up. Similarly, the proportion of women who experienced abdominal pain during the 24 hours following the initial operation and two weeks after the initial operation was higher in the HTA group than in the rollerball group. However, three months after the operation, there was no longer a difference between the two

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[11] See section 2.1.

Table 6

Results of a randomized trial that compared hydrothermal endometrial ablation (HTA) and rollerball endometrial ablation

Outcome measures	HTA	Rollerball ablation	*P*
PATIENT FLOW (n)			
Subjects randomized	n = 187	n = 89	
Procedure not initiated	3	4	
Procedure aborted	7	0	
12 months after the initial intervention			
Reintervention	2	0	
Death[a]	2	0	
Lost to follow-up	6	2	
OPERATIVE DATA	n = 184	n = 85	
Operating time (minutes)[b]	26.4 (± 12.1)	32.2 (± 12.2)	No data
General anesthesia (%)	55.0	76.0	No data
COMPLICATIONS (%)	n = 184	n = 85	
Surgical complications[c]			
24 hours after the operation			No data
Uterine perforation[d]	1.1	2.4	
Abdominal cramping[e]	27.7	24.7	
Abdominal pain	4.3	2.4	
Urinary tract infection	2.7	2.4	
Endometritis	1.1	1.2	
Technical malfunction	3.8	0	
2 weeks after the operation			No data
Uterine perforation[d]	0.5	0	
Abdominal cramping[e]	20.1	12.9	
Abdominal pain	3.3	0	
Urinary tract infection	1.6	0	
Endometritis	0.5	1.2	
Transient alterations in the cervical epithelium	10.3	0	
Thermal injury[f]	0.5	0	
Vaginal infection	0.5	0	
3, 6 and 12 months after the operation			No data
Abdominal cramping[e]	13.6	9.4	
Abdominal pain	1.1	1.2	
Urinary tract infection	0.5	1.2	
Vaginal infection	3.3	2.4	
Hematometra	0.5	2.4	
Need for surgical reintervention			
Repeat ablation	0	0	–
Hysterectomy	1.1	0	No data

[a] Unrelated to the surgical intervention.

[b] Mean (± SD).

[c] Safety data reported by the FDA [2001d]. Nausea and vomiting not included.

[d] Includes cervical laceration.

[e] Other than abdominal pain.

[f] Second-degree burn to upper thigh.

Source: [Corson, 2001; FDA, 2001d]

Table 6 (Cont'd)

Outcome measures	HTA	Rollerball ablation	*P*
TREATMENT OUTCOMES 12 MONTHS AFTER THE INITIAL OPERATION			
Intention-to-treat analysis			
Diary score (%)[g]	**n = 187**	**n = 89**	
≤ 75[h]	68.4	76.4	> 0.05
0[i]	35.3	47.2	> 0.05
Per-protocol analysis			
Diary score (%)	**n = 167**	**n = 83**	
≤ 75	76.6	81.9	> 0.05
0	39.5	50.6	> 0.05
≤ 100[j]	82.0	85.0	> 0.05
Mean reduction[k]	82.3	87.6	No data
Reduction ≥ 90%	67.0	73.0	> 0.05
Quality of life	**n = 167**	**n = 83**	No data
• ***Ruta questionnaire***[l]			
Before treatment	54.2 (± 13.5)	53.3 (± 13.5)	
12 months after treatment	13.0 (± 15.0)	11.4 (± 15.2)	
• ***Effect on leisure activities (%)***			
Before treatment	70.1	66.3	
12 months after treatment	21.6	28.9	
• ***Effect on work and daily activities (%)***			
Before treatment	90.4	91.0	
12 months after treatment	19.8	20.0	

[g] Menstrual blood loss evaluated using pictorial charts.

[h] Primary endpoint.

[i] Amenorrhea.

[j] Uterine bleeding reduced or normalized.

[k] Mean percent reduction in diary scores.

[l] A high score indicates more severe menorrhagia; mean (± SD).

Source: [Corson, 2001 ; FDA, 2001d]

groups in this regard. Cases of asymptomatic alterations in the cervical epithelium, ranging from erythema to shallow ulcerations, occurred in the HTA group. In any event, the cervical epithelium returned to normal within 30 days after the ablation. No medical or surgical treatment was required, and no long-term effects were reported. One woman undergoing hydrothermal ablation experienced a second-degree burn to the upper thigh as a result of prolonged contact between the skin and the HTA tubing. Modifications were subsequently made to the device to reduce the risk of such events recurring. The other postoperative complications reported included endometritis, hematometra, and urinary tract or vaginal infection. These occurred in both groups.

During the 12 months following the initial operation, a hysterectomy was required in two women (1.1%) who had been treated by hydrothermal ablation.

Statistical analyses showed that hydrothermal ablation and rollerball ablation were comparable in terms of efficacy. The therapeutic success rates (diary scores of 75 or less) were clinically and statistically comparable. Twelve months after the initial operation, the amenorrhea rate was higher in the rollerball group than in the hydrothermal group, although the observed difference was not significant. The mean diary score had decreased by 82.3% and 87.6% in the hydrothermal group and rollerball group, respectively.

Based on the evolution in the answers to the quality-of-life questionnaire, the two techniques yielded comparable outcomes. Twelve months after the initial operation, most of the women in both groups indicated that their uterine bleeding had little impact on their quality of life.

The participants in this trial are involved in a 3-year follow-up for assessing the long-term efficacy and safety of hydrothermal endometrial ablation using the HTA [FDA, 2001c].

5.3.2.6 Comparison of cryoablation (Her Option) and rollerball ablation

The results of the only randomized controlled trial, of 12 months' duration, of endometrial cryoablation (Her Option) and rollerball endometrial ablation had not been published as at July 31, 2002 [Heppard et al., 2001]. However, the FDA had examined these results and posted an efficacy and safety data summary on its Web site [FDA, 2001b]. Two hundred and seventy-nine women were randomized at the beginning of the study. In all, 272 of them were eventually treated under the protocol, 186 by cryotherapy and 86 by rollerball.

Menstrual blood loss was evaluated prospectively using a validated pictorial chart method [Higham et al., 1990][12]. Treatment success (primary endpoint) was a reduction in diary scores of at least 150 before treatment to 75 or less one year after the initial intervention. The secondary outcome measure was quality of life, as assessed by means of the SF-36 questionnaire and a modified version of the validated Dartmouth COOP assessment tool. Since the latter does not contain any questions on menorrhagia, the Dartmouth Committee granted approval to use the same style of questions and to format them according to the study design. The outcomes included dysmenorrhea and premenstrual symptom themes found in the SF-36 questionnaire (see Table 7).

The mean operating time is not given. General anesthesia was administered to 45.7% of the cryoablation subjects and 91.9% of the rollerball subjects.

The 49 cases of technical malfunction reported in the cryoablation group were mainly due to console malfunction and did not pose a risk to the patients' safety. Only five malfunctions resulted in acute treatment failure. They delayed cryosurgery in two patients. In three others, treatment could not be initiated, and they were treated with rollerball ablation instead. Corrections were made to the Her Option System in order to eliminate the reliability issues reported during the multicentre clinical trial, and a new clinical trial was undertaken to assess the efficacy of these measures [FDA, 2001a].

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[12] See section 2.1.

Table 7

Results of a randomized trial that compared endometrial cryoablation (Her Option) and rollerball endometrial ablation

Outcome measures	Her Option	Rollerball ablation	*P*[a]
PATIENT FLOW (n)			
Subjects randomized	n = 193	n = 86	
Procedure not initiated	4	0	
Procedure aborted	3	0	
12 months after the initial intervention			
Reintervention	6	3	
Lost to follow-up	15	9	
OPERATIVE DATA	n = 186	n = 86	
Operating time (minutes)	No data	No data	–
General anesthesia (%)	45.7	91.9	No data
COMPLICATIONS (%)	n = 186	n = 86	
Surgical complications[b]			
24 hours after the operation			No data
Uterine perforation[c]	0.5	2.3	
Fluid overload[d]	0	3.5	
Uterine cramping	8.1	4.7	
Other abdominal or pelvic pain/cramping	14.5	11.6	
Hot flashes	1.1	0	
Technical malfunction	25.9[e]	0	
2 weeks after the operation			No data
Uterine cramping	2.7	0	
Other abdominal or pelvic pain/cramping	3.8	9.3	
Hot flashes	3.2	3.5	
Urinary tract infection	2.7	3.5	
Vaginal infection	1.1	1.2	
3, 6 and 12 weeks after the operation			No data
Uterine cramping	3.8	5.8	
Other abdominal or pelvic pain/cramping	14.0	18.6	
Hot flashes	1.6	8.1	
Urinary tract infection	1.1	3.5	
Vaginal infection	3.8	1.2	
Pregnancy	0.5	0	
Heavy uterine bleeding[f]	≤ 1.0	0	
Need for surgical reintervention			
Repeat ablation	0	0	–
Hysterectomy	3.2	3.5	No data

[a] The FDA does not report the results of the statistical analyses (*P* values).

[b] Nausea and vomiting not included.

[c] Includes cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

[e] 49 technical malfunctions in 189 hydrothermal ablations (including 3 malfunctions that prevented initiation of treatment).

[f] More than two weeks after the initial operation; number of cases not reported.

Source: [FDA, 2001b]

Table 7 (Cont'd)

Outcome measures	Her Option	Rollerball ablation	*P*[a]
TREATMENT OUTCOMES 12 MONTHS AFTER INITIAL OPERATION			
Intention-to-treat analysis			
Diary score (%)[g]	**n = 193**	**n = 86**	No data
≤ 75[h]	67.4	73.3	
0[i]	22.2	46.5	
Per-protocol analysis			
Diary score (%)	**n = 174**	**n = 77**	No data
≤ 75	74.7	81.8	
0[j]	24.7	51.9	
Quality of life	**n = 157**	**n = 73**	
• ***Questionnaire***[k]			No data
Before treatment	3.4 (± 1.0)	3.4 (± 0.9)	
12 months after treatment	1.3 (± 0.7)	1.3 (± 0.9)	
• ***Time lost from work or other activities due to menstruation (%)***			No data
Before treatment	74.0	71.0	
12 months after treatment	6.0	7.0	
• ***Satisfaction and acceptability (%)***			No data
Very or extremely satisfied	86.0	88.0	
Would recommend the treatment to other women	98.0	95.0	

[a] The FDA does not report the results of the statistical analyses (*P* values).

[g] Menstrual blood loss evaluated using pictorial charts.

[h] Primary endpoint.

[i] Amenorrhea.

[j] Results calculated by the main author of this report.

[k] Scale of 1 to 5. A high value indicates a greater effect; mean (± SD).

Source: [FDA, 2001b]

No serious complications occurred in either group. One case of uterine perforation occurred during hysterometry prior to cryoablation and another during rollerball ablation. One case of cervical laceration occurred as well in the rollerball group. Three women absorbed more than 1.5 L of irrigation fluid during rollerball ablation. The post-operative complications observed in the two groups included uterine cramping, abdominal or pelvic pain/cramping, hot flashes and urinary tract or vaginal infection. Heavy uterine bleeding (more than two weeks after the operation) and one pregnancy occurred in no more than 1% of the women treated by cryoablation.

A hysterectomy was required in six women (3.2%) in the cryoablation group and three (3.5%) in the rollerball group during the 12 months following the initial operation.

Cryoablation seemed to be as effective as rollerball ablation. The treatment success rates (diary score of 75 or less) were clinically similar. However, twice as many women treated by rollerball ablation than cryoablation were amenorrheic 12 months after the initial operation. Unfortunately, since the FDA does not report the results of the two statistical analyses (*P* values), we are unable to say if the results were or were not statistically different. It is interesting to note that the statistical analysis of the subjects treated under the protocol reveals variable success rates at the 10 participating centres. The treatment success rate 12 months after the initial operation ranged from 44 to 90% in the cryoablation group and 40 to 100% in the other group. A second clinical trial was undertaken to examine the standardization of the endometrial cryoablation technique to determine whether certain variations in surgical technique could alter the efficacy of the Her Option System [FDA, 2001a; Sanders, 2001].

The satisfaction and treatment acceptability rates 12 months after the initial intervention were high in both groups. The proportion of women extremely or very satisfied with the treatment outcomes was similar in both groups. In addition, most of the participants considered the treatments acceptable and would recommend them to other women. Based on the evolution in the answers to the quality-of-life questionnaire, the two techniques yielded comparable outcomes. Twelve months after the initial operation, most of the women in both groups indicated that their uterine bleeding had little impact on their quality of life. Both techniques led to a substantial reduction in time lost from work or other activities due to menstruation.

The participants in this trial are involved in a 3-year follow-up aimed at assessing the long-term efficacy and safety of endometrial cryoablation using the Her Option System [FDA, 2001a].

5.3.2.7 Comparison of impedance-controlled ablation (NovaSure) and transcervical resection

The results of the only randomized, controlled trial, of 12 months' duration, of impedance-controlled endometrial ablation (NovaSure) and transcervical resection of the endometrium (with treatment of the uterine fundus and cornual regions with a rollerball electrode) had not been published as at July 31, 2002. However, the FDA had examined these results and posted an effectiveness and safety data summary on its Web site [FDA, 2000f]. In all, 265 women were randomized and treated under the protocol, 175 by impedance-controlled ablation and 90 by transcervical resection.

Menstrual blood loss was evaluated prospectively using a validated pictorial chart method [Higham et al., 1990][13]. Treatment success (primary endpoint) was a reduction in diary scores of at least 150 before treatment to 75 or less one year after the initial intervention. The secondary outcome measures were procedure time, patient satisfaction (as recorded by patient self-reporting using quality-of-life and menstrual impact scales) and amenorrhea rates. The safety assessment of the treatments was based on complications and adverse events reported during the clinical trial, including malfunctions of the NovaSure (see Table 8).

The mean procedure time for impedance-controlled ablation was much shorter than that for transcervical resection. General anesthesia or epidural

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[13] See section 2.1.

Table 8

Results of a randomized trial that compared impedance-controlled endometrial ablation (NovaSure) and transcervical resection of the endometrium

Outcome measures	NovaSure	Transcervical resection[a]	P[b]
PATIENT FLOW (n)			
Subjects randomized	n = 175	n = 90	
Procedure aborted	4	2	
12 months after the initial intervention			
Additional treatment	7	4	
Lost to follow-up	6	2	
Excluded from study	2	0	
OPERATIVE DATA	n = 175	n = 90	
Operating time (minutes)[c]	4.2 (± 3.5)	24.2 (± 11.4)	No data
General anesthesia or epidural (%)	27.0	82.2	No data
COMPLICATIONS (%)	n = 175	n = 90	
Intraoperative complications			No data
Uterine perforation[d]	0	5.6	
Cervical stenosis	0	1.1	
Bradycardia	0.6	0	
Technical malfunction	13.7[e]	0	
Postoperative complications[f]			
≤ 24 hours after the operation			No data
Pelvic pain/cramping	3.4	4.4	
> 24 hours to 2 weeks after the operation			No data
Pelvic pain/cramping	0.6	1.1	
Hematometra	0.6	0	
Endometritis	0	2.2	
Hemorrhage	0	1.1	
Urinary tract infection	0.6	1.1	
Vaginal infection	0.6	0	
Pelvic inflammatory disease	0	1.1	
> 2 weeks to 12 months after the operation			No data
Pelvic pain/cramping	2.9	6.7	
Hematometra	0.6	2.2	
Endometritis	1.1	1.1	
Hemorrhage	0.6	0	
Urinary tract infection	1.1	2.2	
Vaginal infection	2.9	2.2	
Pelvic inflammatory disease	1.1	0	
Need for further treatment			No data
Hysterectomy	1.7	2.2	
Other[g]	2.3	2.2	

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[b] The FDA does not report the results of the statistical analyses (*P* values).

[c] Mean (± SD). Procedure time was measured from when the disposable device or resectoscope was inserted into the uterine cavity until it was removed.

[d] Includes cervical laceration.

[e] 24 technical malfunctions in 175 impedance-controlled ablations (no aborted procedures).

[f] Nausea and vomiting not included.

[g] Not specified.

Source: [FDA, 2001f]

Table 8 (Cont'd)

Outcome measures	NovaSure	Transcervical resection[a]	*P*[b]
TREATMENT OUTCOMES 12 MONTHS AFTER THE INITIAL OPERATION			
Intention-to-treat analysis			
Diary score (%)[h]	n = 175	n = 90	No data
≤ 75[i]	77.7	74.4	
0[j]	36.0	32.2	
Per-protocol analysis			
Diary score (%)	n = 156	n = 82	No data
≤ 75[k]	87.2	81.7	
0[k]	40.4	35.4	
Quality of life (%)	n = 154	n = 82	
• ***Premenstrual syndrome***			No data
Before treatment	66.2	65.9	
12 months after treatment	36.4	35.4	
• ***Dysmenorrhea***			No data
Before treatment	55.8	56.1	
12 months after treatment	20.8	34.1	
• ***Satisfaction and acceptability***			No data
Satisfied or very satisfied	91.6	92.7	
Would definitely or probably recommend the treatment to other women	94.8	95.1	

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[b] The FDA does not report the results of the statistical analyses (*P* values).

[h] Menstrual blood loss evaluated by the pictorial chart method.

[i] Primary endpoint.

[j] Amenorrhea.

[k] Results calculated by the main author of this report.

Source: [FDA, 2001f]

was administered to 27% and 82% of the women treated by impedance-controlled ablation and those treated by transcervical resection, respectively.

All 24 cases of technical malfunction reported in the impedance-controlled ablation group involved the disposable device unit and did not pose a risk to the patients' safety. The clinical investigators determined that 23 of these units could not be used and returned them to the manufacturer. Another unit was returned after successful use because the investigator had complained that the locking mechanism was difficult to adjust. In no case did a technical malfunction result in a patient not being treated.

One (0.6%) and six (6.7%) intraoperative complications occurred in the impedance-controlled group and the transcervical resection group, respectively. The potentially serious complications of transcervical resection included three cases of uterine perforation and two cases of cervical laceration. The postoperative complications observed in both groups included endometritis, hematometra, hemorrhage, urinary tract infection, pelvic inflammatory disease and vaginal infection.

The proportion of women who required surgical reintervention after failure of the initial operation was comparable in both groups. During the 12 months following the initial operation, three women (1.7%) in the impedance-controlled group and two (2.2%) in the transcervical resection group, respectively, required a hysterectomy.

Impedance-controlled ablation seemed as clinically effective as transcervical resection. Twelve months after the initial surgery, the diary score was 75 or less in 77.7% and 74.4% of the women treated by impedance-controlled ablation and transcervical resection, respectively. The amenorrhea rate was comparable in both groups. Unfortunately, since the FDA does not report the results of the two statistical analyses (*P* values), we are unable to say if the results were or were not statistically different.

Twelve months after the initial operation, the satisfaction and treatment acceptability rates were high in both groups. The proportion of women who were satisfied or very satisfied with the surgical treatment was similar in both groups. In addition, most of the participants considered the treatments acceptable and would recommend them to other women. Both techniques led to comparable reductions in the incidence of premenstrual syndrome. Transcervical resection resulted in a smaller decrease in the incidence of dysmenorrhea than impedance-controlled ablation.

The participants in this trial are involved in a 3-year follow-up aimed at assessing the long-term efficacy and safety of impedance-controlled endometrial ablation using the NovaSure System [FDA, 2000e].

5.3.2.8 National, prospective survey for assessing the safety of endometrial ablation techniques

As part of the MISTLETOE survey [Overton et al., 1997], clinical data on more than 10,000 endometrial ablations performed in England, Wales and Northern Ireland between April 1993 and October 1994 were closely examined. The study compared different endometrial ablation techniques, specifically, laser ablation, transcervical resection, rollerball ablation and combined diathermy (transcervical resection together with treatment of the uterine fundus and cornual regions with a rollerball electrode).

The intraoperative complications reported included hemorrhage, uterine perforation, cardiovascular or respiratory complications, visceral burn, and emergency interventions, such as hysterectomy, laparotomy, laparoscopy and surgical repair of cervical lacerations (see Table 9).

A statistical analysis showed that the operating time was comparable in the four main groups, although transcervical resection took statistically significantly less time. The absorption of more than 2 L of irrigation fluid occurred much more frequently in the laser-treated group.

The four main techniques examined in this large cohort were associated with an overall intraoperative complication rate of 4.44% and required emergency intervention in 1.25% of the subjects. The laser and rollerball-treated women experienced significantly fewer intraoperative complications. Combined diathermy caused significantly fewer immediate complications than transcervical resection. The probability of emergency intervention was lower in the laser-treated patients. There were very few postoperative complications (rate: 0.77 to 2.86%) or complications up to six weeks after surgery

Table 9

Results of the prospective survey conducted in the United Kingdom for the purpose of evaluating the safety of endometrial ablation techniques

Safety Results									
Technique	N	Procedure time (minutes)	Fluid overload >2 L (%)	Intraoperative complication rate (%)					
				Uterine perforation	Hemorrhage	Cardiovascular or respiratory	Visceral burn	Total[a]	Emergency intervention[b]
Laser ablation	1,793	31.5	5.1[c]	0.6	1.2	0.5	0	2.7[d,e]	0.34[e]
Transcervical resection	3,776	24.9[f]	1.5	2.4	3.4	0.5	0.1	6.4	2.39
Rollerball ablation	650	30.4	1.2	0.6	1.0	0.5	0	2.1[e]	1.11
Combined diathermy[g]	4,291	27.9	1.0	1.2	2.4	0.5	0.1	4.2[h]	1.36[h]

[a] The overall frequency of intraoperative complications, excluding fluid overload and emergency interventions.

[b] Includes hysterectomy, laparoscopy, laparotomy and cervical lacerations requiring surgical repair.

[c] Technique associated with the highest incidence ($P < 0.01$).

[d] Includes seven intraoperative complications not specified by the authors.

[e] $P < 0.01$; comparison with transcervical resection and combined diathermy.

[f] The fastest technique ($P < 0.01$).

[g] Transcervical resection combined with treatment of the uterine fundus and cornual regions with a rollerball electrode.

[h] $P < 0.01$; comparison with transcervical resection.

Source: [Overton et al., 1997]

(rate: 1.25 to 4.58%). In neither case did the difference reach the significance threshold of 1%.

Combined diathermy and transcervical resection were associated with a mortality rate of two and three per 10,000 patients, respectively.

One of the main objectives of this survey was to examine the relationship between surgical experience and the frequency of complications. The results indicate that not having taken any training courses has no effect on the frequency of intraoperative complications. The investigators did not succeed in determining the level of experience necessary for using these techniques, except in the case of transcervical resection, where the frequency of complications diminished with surgical experience.

Actually, the authors recommend that transcervical resection (performed solely with a metal loop) be abandoned because of the high incidence of complications. Since this survey did not examine the follow-up data, it does not give the treatment outcomes.

5.4 Recapitulation

The results of studies that have evaluated endometrial ablation techniques in the treatment of dysfunctional uterine bleeding are briefly presented in Tables 10 and 11. It should be noted that the studies differed considerably in terms of design, the inclusion and exclusion criteria, preparation of the uterus, or the methods used to evaluate menstrual blood loss, quality of life or satisfaction with the surgical treatment. Although long-term data are available, they are from nonrandomized or uncontrolled studies, while the data from the follow-ups conducted after the randomized, controlled trials cover a short period of time.

Menstrual blood loss and dysmenorrhea can increase with time after endometrial ablation [NHSCRD, 1995]. The efficacy and the reintervention rates reported in the studies therefore depend on the duration of the posttreatment follow-up [Lethaby et al., 2000d]. The reintervention rates reported varied from 0 to 38.2%, with the highest rates observed in the longer studies. A direct comparison of the results may therefore be difficult, since the study population, methodology and study outcome measures may have varied from study to study.

The three first-generation ablation techniques require direct visual monitoring, using a hysteroscope, of the uterine cavity irrigated with a solution. The monitoring also serves to diagnose and treat intrauterine diseases, such as submucous uterine fibroids and polyps. Even if the uterine cavity seems normal on hysteroscopic examination, a small piece of the endometrium should be removed, since hysteroscopy alone cannot rule out the possibility of neoplasm or endometrial carcinoma [Vilos et al., 2001]. These techniques are sometimes referred to as hysteroscopic endometrial ablation techniques.

The first-generation endometrial ablation techniques offer considerable advantages over hysterectomy. They take less time to perform and result in a much shorter hospital stay and recovery. Although hysterectomy guarantees the cessation of menstrual blood loss and yields a higher level of satisfaction, it does carry a greater risk of complications than endometrial ablation.

Compared to the first-generation ablation techniques, the second-generation techniques assessed in this report offer the advantage of being quick and easy to perform and amenable to local anesthesia or narcosis and of causing fewer intraoperative complications. However, they do carry a risk of complications, including hematometra, infection and injury to internal organs. It would be useful to examine these techniques further to determine their cost-effectiveness and to confirm their safety when performed by a gynecologist who has not received special training (in the event that they are performed in clinics). It should be noted that the cervix has to be dilated to 8 mm (hydrothermal ablation and impedance-controlled ablation) or 9 mm (microwave ablation) and that the dilatation process can be painful, even with local anesthesia.

As with any other technique performed without direct visual monitoring, the main concern with the second-generation ablation techniques is the risk of an accidental perforation and of subsequent bowel injury. In the United Kingdom, the Medical Devices Agency (MDA) received reports of serious accidents involving mainly the bowel that had occurred during endometrial ablations by various heat-based techniques (heated normal saline, microwaves, etc.). The incidence of this problem increases when the bowel is in contact with the uterine wall or when the latter is thinner than expected. In addition to the hysterosonography mentioned in notice SN9812 [MDA, 1998], the MDA recommends that a hysteroscopy be performed before inserting the applicator, regardless of which device is used, except for thermal balloon ablation devices [MDA, 1999]. The purpose of this is to ensure that the hysterometry and dilatation of the cervix do not cause a perforation or false passage. It is also advisable to perform a hysteroscopy after the treatment to check that only the uterine cavity was treated [Vilos et al., 2001].

Table 10
Efficacy of endometrial ablation techniques: Summary of study results

Efficacy results[a] for the first-generation techniques								
Technique	Study	N[b]	Duration of follow-up	Percent change in menstrual blood loss[c]				Satisfaction rate[g] (%)
				Amenorrhea	Hypomenorrhea[d]	Diary score ≤ 75[e]	Failure[f]	
Laser ablation	Uncontrolled	11	3 months to 11 years	23.0 to 81.4	18.6 to 77.0	No data	0 to 8.6	83.4 to 97.3
	Case-control	1	6 months to 4 years	87.2 to 96.4[h]	87.2 to 96.4[h]	No data	3.6 to 12.8[h]	No data
	Nonrandomized, controlled	1	No data	No data	No data	No data	No data	No data
	Randomized, controlled	1	12 months	23.1	49.4	No data	5.6	89.2
Transcervical resection[i]	Uncontrolled	11	3 months to 5 years	8.0 to 94.4	5.6 to 75.5	No data	0 to 28.0	63.0 to 100
	Case-control	2	3 months to 4 years	37.8 to 70.9	25.6 to 44.6	No data	3.5 to 17.6	No data
	Nonrandomized, controlled	2	3 to 24 months	17.0 to 36.0[h,j]	No data	No data	No data	43.0 to 80.0[h,j]
	Randomized, controlled	6[k,l]	12 to 72 months	21.9 to 68.0	46.6 to 51.6	81.7[j]	3.0 to 10.9	67.0 to 100
	Meta-analysis	1	1 to 4 years	86.6 to 97.3[h]	86.8 to 97.3[h]	No data	2.7 to 13.2[h]	80.3 to 89.0[h]
Rollerball ablation	Uncontrolled	12	0.25 months to 11years	25.0 to 60.0	35.0 to 69.0	No data	0 to 16.2	78.8 to 87.8
	Case-control	3	6 to 68 months	43.8 to 70.9	25.6 to 40.0	No data	3.5 to 15.4	78.8 to 85.0
	Nonrandomized, controlled	1	No data	No data	No data	No data	No data	No data
	Randomized, controlled	4	12 to 60 months	21.9 to 51.9	34.4 to 68.6	81.8 to 84.3	6.0 to 9.5[j,m]	88.0 to 99.1

[a] Per-protocol statistical analysis.

[b] Number of published studies (including the studies that compared endometrial ablation techniques with hysterectomy and the prospective survey conducted in the United Kingdom).

[c] After the first endometrial ablation.

[d] Includes spotting and eumenorrhea.

[e] Menstrual blood loss evaluated using pictorial charts (Higham's or Janssen's diary score); primary outcome measure in recent clinical trials (treatment success is a reduction in diary scores of at least 150 before treatment to 75 or less one year after the initial intervention).

[f] Menstrual blood loss unchanged or heavier.

[g] Includes patients perfectly, completely, extremely, very, generally or moderately satisfied or satisfied.

[h] Depending on the duration of follow-up.

[i] Metal loop used alone or together with a rollerball electrode in the cornual regions and uterine fundus (combined diathermy).

[j] Only one published study provides data on this efficacy criterion.

[k] Two of these studies were randomized, controlled trials of the ablation technique with and without pretreatment with endometrial thinning agents.

[l] The results of five other randomized, controlled trials were included in the meta-analysis.

[m] Failure rate of 9.5% and 6% after 24 and 36 months of follow-up, respectively.

Table 10 (Cont'd)

Efficacy results[a] for the second-generation techniques								
Technique	Study	N[b]	Duration of follow-up	Percent change in menstrual blood loss[c]				Satisfaction rate[g] (%)
				Amenorrhea	Hypomenorrhea[d]	Diary score ≤ 75[e]	Failure[f]	
Thermal balloon ablation (ThermaChoice)	Uncontrolled	9	2 to 34 months	3.3 to 54.5	44.4 to 76.9	No data	0 to 23.3	81.0 to 84.6[n]
	Case-control	1	3 to 44 months	24.7	60.2	No data	15.1	No data
	Nonrandomized, controlled	1	3 to 24 months	13.0 to 17.0[h]	No data	No data	No data	60.0 to 66.0[h]
	Randomized, controlled	2[o]	6 to 36 months	13.1 to 23.5	76.2 to 78.1	80.2[n]	0 to 10.7	84.6 to 96.0
Microwave ablation (MEA)	Uncontrolled	4	6 months to 4 years	18.8 to 56.5	26.1 to 74.9	No data	6.3 to 17.4	82.2 to 87.5
	Randomized, controlled	1	12 to 24 months	39.7 to 47.5	45.8 to 52.5	No data	6.7 to 7.8	76.7 to 79.0
Hydrothermal ablation (HTA)	Uncontrolled	5	3 to 18 months	32.0 to 84.6	15.4 to 64.0	No data	0 to 14.0	92.3 to 96.0
	Randomized, controlled	1	12 months	39.5	42.5	76.6	18.0	No data
Cryoablation (Her Option)	Randomized, controlled	1	12 months	24.7	No data	74.7	No data	86.0
Impedance-controlled ablation (NovaSure)	Randomized, controlled	1	12 months	40.4	No data	87.2	No data	91.6

[a] Per-protocol statistical analysis.

[b] Number of published studies (including the studies that compared endometrial ablation techniques with hysterectomy and the prospective survey conducted in the United Kingdom).

[c] After the first endometrial ablation.

[d] Includes spotting and eumenorrhea.

[e] Menstrual blood loss evaluated using pictorial charts (Higham's or Janssen's diary score); primary outcome measure in recent clinical trials (treatment success is a reduction in diary scores of at least 150 before treatment to 75 or less one year after the initial intervention).

[f] Menstrual blood loss unchanged or heavier.

[g] Includes patients perfectly, completely, extremely, very, generally or moderately satisfied or satisfied.

[h] Depending on the duration of follow-up.

[n] Only two published studies provide data on this efficacy criterion.

[o] One of these studies was a randomized, controlled trial of the ablation technique with and without pretreatment with endometrial thinning agents.

Table 11

Safety of endometrial ablation techniques: Summary of study results

Safety results for the first-generation techniques									
Technique	Study[a]	Reintervention rate (%)		Complication rate[c] (%)					
				Intraoperative complications[d]				Postoperative complications	Total
		Repeat EA[b]	Hysterectomy	Uterine perforation[e]	Fluid overload[f]	Hemorrhage	Thermal injury		
Laser ablation	Uncontrolled	1 r: 1.5 to 14.3 2 r: 0.2 to 0.6	0 to 14.6	0 to 1.6	0 to 5.0	0 to 3.9	0[g]	0 to 29.2	0.8 to 29.2
	Case-control	3.6[h]	2.1	1.7	10.3	0	0	0	12.0
	Nonrandomized, controlled	No data	No data	0.6	5.1[i]	1.2	0	No data	7.8[j,k]
	Randomized, controlled	11.2	4.8	0	8.1	3.8	1.1	5.9	18.9
Transcervical resection[l]	Uncontrolled	1 r: 2.0 to 17.5 2 r: 0.3 to 1.3	0 to 9.0	0 to 3.8	0 to 3.8	0 to 14.3	0	0 to 5.0	0 to 17.2
	Case-control	1.3 to 3.5[h]	0 to 6.8	0	0 to 2.0	0	0	0 to 2.7	2.0 to 2.7
	Nonrandomized, controlled	5.3[m]	20.0[m]	1.2 to 2.4	1.0[i] to 4.0	1.3 to 3.4	0 to 0.1	No data	5.2[j,k] to 7.9[j,k]
	Randomized, controlled	0 to 16.9	0 to 13.6	0 to 5.6	0 to 1.7	0 to 3.7	0	6.0 to 14.3[n,o]	5.1[j] to 19.9[o]
	Meta-analysis	14.0 to 38.2[p]	14.0 to 38.2[p]	1.0	11.4	3.6	0	20.3	36.3

[a] Includes the studies that compared endometrial ablation techniques with hysterectomy and the prospective survey conducted in the United Kingdom. See Table 10 for the number of published studies and the durations of follow-up.

[b] EA: endometrial ablation; r: repeat.

[c] All endometrial ablations combined (initial interventions and repeats).

[d] Excluding technical malfunctions and aborted procedures.

[e] Includes cervical laceration.

[f] Fluid absorption ≥ 1.5 L.

[g] Cases of bowel injury reported in the literature.

[h] Six months after the initial operation. No data after four years of follow-up.

[i] Fluid absorption > 2 L.

[j] Intraoperative complications only.

[k] Overall intraoperative complication rate reported in the prospective survey conducted in the United Kingdom. Includes the cases of fluid absorption > 2 L.

[l] Metal loop used alone or together with a rollerball electrode in the cornual regions and uterine fundus (combined diathermy).

[m] Only one published study provides data on this.

[n] Includes cervical stenosis.

[o] Does not include nausea or vomiting; uterine, abdominal or pelvic pain/cramping; or hot flashes [FDA, 1997; FDA 2001b; FDA 2001d; FDA, 2001f].

[p] Depending on the duration of follow-up.

Table 11 (Cont'd)

Safety results for the first-generation techniques									
Technique	Study[a]	Reintervention rate (%)		Complication rate[c] (%)					
				Intraoperative complications[d]				Postoperative complications	Total
		Repeat EA[b]	Hysterectomy	Uterine perforation[e]	Fluid overload[f]	Hemorrhage	Thermal injury		
Rollerball ablation	Uncontrolled	0 to 11.5	1.4 to 34.1	0 to 4.3	0 to 2.6	0 to 1.3	0[q]	0 to 3.8	0 to 8.3
	Case-control	3.1 to 9.1[h]	8.8 to 11.1	0 to 2.5	0 to 3.1	0 to 1.3	0	0 to 3.1	0 to 7.8
	Nonrandomized, controlled	No data	No data	0.6	1.2[i]	1.0	0	No data	3.3[j,k]
	Randomized, controlled	0 to 16.4	0 to 16.4	1.6 to 2.4	0 to 3.5	0	0	2.4[o] to 14.8[r]	5.6[o] to 15.2[o]

[a] Includes the studies that compared endometrial ablation techniques with hysterectomy and the prospective survey conducted in the United Kingdom. See Table 10 for the number of published studies and the durations of follow-up.

[b] EA: endometrial ablation; r: repeat.

[c] All endometrial ablations combined (initial interventions and repeats).

[d] Excluding technical malfunctions and aborted procedures.

[e] Includes cervical laceration.

[f] Fluid absorption ≥ 1.5 L.

[h] Six months after the initial operation. No data after four years of follow-up.

[i] Fluid absorption > 2 L.

[j] Intraoperative complications only.

[k] Overall intraoperative complication rate reported in the prospective survey conducted in the United Kingdom. Includes cases of fluid absorption ≥ 2 L.

[o] Does not include nausea or vomiting; uterine, abdominal or pelvic pain/cramping; or hot flashes [FDA, 1997; FDA 2001b; FDA 2001d; FDA, 2001f].

[q] Cases of thermal injury to the genitals reported in the literature.

[r] Includes one case of serious infection (resulting in death due to disseminated intravascular coagulation three days after the operation).

Table 11 (Cont'd)

Safety results for the second-generation techniques									
Technique	Study[a]	Reintervention rate (%)		Complication rate[c] (%)					
				Intraoperative complications[d]				Postoperative complications	Total
		Repeat EA[b]	Hysterectomy	Uterine perforation[e]	Fluid overload[f]	Hemorrhage	Thermal injury		
Thermal balloon ablation (ThermaChoice)	Uncontrolled	0 to 36.7	0 to 15.4	0[s]	0	0	0	0 to 15.4	0 to 15.4
	Case-control	0	9.6	0	0	0	0	1.4	1.4
	Nonrandomized, controlled	0	11.7	0	0	0	0	No data	0[i]
	Randomized, controlled	0 to 0.8	1.5 to 15.3	0	0	0	0	4.3[o] to 5.0	4.3[o] to 5.0
Microwave ablation (MEA)	Uncontrolled	0 to 13.0	0 to 11.0	0 to 0.3	0	0	0[g]	0.9 to 25.1	1.2 to 25.1
	Randomized, controlled	0.8	7.0 to 11.6	0.8	0	0	0	0.8[t]	1.6[t]
Hydrothermal ablation (HTA)	Uncontrolled	0 to 7.7	3.8 to 7.1	0	0	0	0 to 3.1[g]	0 to 25.0	0 to 25.0
	Randomized, controlled	0	1.1	1.6	0	0	0.5[u]	21.0[o]	23.1[o]
Cryoablation (Her Option)	Randomized, controlled	0	3.2	0.5	0	0	0	10.2[o]	10.7[o]
Impedance-controlled ablation (NovaSure)	Randomized, controlled	No data[v]	1.7	0	0	0	0	9.8[o,w]	9.8[o]

[a] Includes the studies that compared endometrial ablation techniques with hysterectomy and the prospective survey conducted in the United Kingdom. See Table 10 for the number of published studies and the durations of follow-up.

[b] EA: endometrial ablation; r: repeat.

[c] All endometrial ablations combined (initial interventions and repeats).

[d] Excluding technical malfunctions and aborted procedures.

[e] Includes cervical laceration.

[f] Fluid absorption ≥ 1.5 L.

[g] Cases of bowel injury reported in the literature.

[i] Intraoperative complications only.

[o] Does not include nausea or vomiting; uterine, abdominal or pelvic pain/cramping; or hot flashes [FDA, 1997; FDA 2001b; FDA 2001d; FDA, 2001f].

[s] One case of uterine perforation has been reported worldwide (approximately 3,000 women treated with the ThermaChoice).

[t] No postoperative complications reported during the 12 months following the initial intervention.

[u] A second-degree burn to the upper thigh as a result of prolonged contact between the skin and the HTA tubing.

[v] 2.3% of the women required additional treatment (not specified) after treatment failure.

[w] Includes bradycardia (occurred during treatment).

6

STATUS OF ENDOMETRIAL ABLATION TECHNIQUES IN THE TREATMENT OF DYSFUNCTIONAL UTERINE BLEEDING

6.1 First-generation techniques

6.1.1 Transcervical resection

In accordance with the Agency's terminology and criteria, transcervical resection of the endometrium is considered an accepted technique [CETS, 1998]. The results of a meta-analysis, of six randomized, controlled trials and of several other studies indicate that this technique is safe, with reproducible results. It is relatively effective in reducing the quantity of menstrual blood loss and yields a high level of satisfaction. Some of the advantages of transcervical resection include the possibility of performing an endometrial biopsy in order to rule out the presence of a neoplasm and the possibility of surgically removing intrauterine lesions, such as polyps and leiomyomas. On the other hand, this technique requires a high level of surgical skill and carries a greater risk of uterine perforation and systemic absorption of irrigation fluid as a result of blood vessel exposure. However, transcervical resection of the endometrium causes few serious complications, especially if a rollerball electrode is used to treat the uterine fundus and cornual regions (combined diathermy). Of the contraindications to transcervical resection of the endometrium, particular mention should be made of hemodynamic instability, coagulopathies and anticoagulant therapy.

6.1.2 Rollerball ablation

Rollerball endometrial ablation is an accepted technique as well. Based on published studies, it seems to compare with transcervical resection in terms of efficacy, the level of satisfaction and the reoperation rate. It is the easiest first-generation technique to master and the quickest to perform. Rollerball endometrial ablation causes fewer intraoperative complications than transcervical resection [Overton et al., 1997]. It carries a lower risk of uterine perforation and fluid absorption, since the tip of the rollerball is blunt. This technique is especially indicated for uterine bleeding secondary to anticoagulant therapy.

6.1.3 Laser ablation

Based on published studies, laser endometrial ablation seems comparable to transcervical resection in terms of efficacy, the level of satisfaction and the reoperation rate. The main drawbacks of laser ablation are the cost and length of the procedure. Furthermore, this technique requires more surgical skill, but it causes fewer intraoperative complications than transcervical resection of the endometrium [Overton et al., 1997]. In Québec, laser endometrial ablation stopped being performed about ten years ago.

6.2 Second-generation techniques

6.2.1 Thermal balloon ablation

Of the second-generation ablation techniques, only thermal balloon endometrial ablation is considered accepted. Based on the long-term results of a randomized, controlled trial and those of several other studies, this technique seems comparable to transcervical resection in terms of efficacy and the reoperation rate. Very few studies have examined the level of satisfaction with this treatment. However, thermal balloon ablation has been compared with rollerball ablation. Thermal balloon ablation is quick and easy to perform and causes few intraoperative complications. It seems to be reserved for normal uterine cavities and causes pain because of uterine distention. The risk of treatment failure is greater in the presence of uterine retroversion. Among the contraindications to thermal balloon ablation, particular mention should be made of an active genital or urinary tract infection or any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy. When this report was being drafted, the use of thermal balloon ablation was still not very widespread in Québec.

6.2.2 Microwave ablation

We have fewer data on microwave endometrial ablation than on the first-generation techniques or thermal balloon endometrial ablation. Based on the medium-term results of a randomized, controlled trial and those of a few uncontrolled clinical studies, microwave ablation seems comparable to transcervical resection in terms of efficacy, the level of satisfaction and the reintervention rate. It is easy and quick to perform and causes few intraoperative complications. However, as of yet, no long-term results of large, randomized, controlled trials have been published. Such results would enable us to better assess the impact of the therapeutic effects and, more specifically, the reoperation rate, which seems to plateau within three years after the initial procedure [O'Connor and Magos, 1996]. This is why this technique is considered innovative. There is the potential for microwave ablation to be incomplete in women with an enlarged (at least 12 cm in length) and highly deformed uterine cavity. It should be noted that the cervix has to be dilated to 9 mm in order to insert the waveguide and that the dilatation process can be painful, even with local anesthesia.

6.2.3 Hydrothermal ablation

Hydrothermal endometrial ablation is considered an innovative technique as well. We have few data on this technique, and no long-term results of large, randomized, controlled trials have been published. Based on the results of a randomized, controlled trial and of a few uncontrolled clinical studies, it seems that this technique compares with transcervical resection in terms of efficacy and the reintervention rate. Few studies have examined the level of satisfaction with hydrothermal ablation. However, comparisons have been done of this technique and rollerball ablation. Hydrothermal ablation is quick and easy to perform and causes few intraoperative complications. The diagnostic hysteroscopy performed prior to treatment enables the physician to check that there are no uterine perforations and to detect any intrauterine pathology not previously diagnosed. Controlled irrigation of the uterine cavity (including the cornual regions) with heated normal saline can reportedly be used to treat benign tumors that are sometimes present in the uterus. It is important to carefully select candidates for this operation, since a large fibroid deforming the uterine cavity would prevent adequate irrigation. Among the contraindications to hydrothermal endometrial ablation, particular mention should be made of an active genital or urinary tract infection and any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy. It should be noted that the cervix has to be dilated to 8 mm in order to insert the device and that the dilatation process can be painful, even with local anesthesia.

6.2.4 Cryoablation

Endometrial cryoablation is also considered an innovative technique. We have few data on this technique, and no long-term results of large, randomized, controlled trials have been published. Based on the results of one randomized, controlled trial, endometrial cryoablation compares with transcervical resection of the endometrium in terms of efficacy, the level of satisfaction and the reintervention rate. However, the trial in question compared cryoablation and rollerball ablation. Cryoablation is quick and easy to perform and causes few intraoperative complications. Hysterosonography is performed to check that the cryoprobe is properly positioned in the uterine cavity and to monitor the growth of the iceball during the treatment cycles. Uterine fibroids do not seem to affect the growth of the iceball and are easily destroyed by freezing. Endometrial cryoablation is especially contraindicated in the presence of an active genital or urinary tract infection and any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy.

6.2.5 Impedance-controlled ablation

Impedance-controlled endometrial ablation is considered an innovative technique as well. As with cryoablation, we have few data on this technique, and no long-term results of large, randomized, controlled trials have been published. Based on the results of one randomized, controlled trial, this technique seems comparable to transcervical resection in terms of efficacy, the satisfaction rate and the reintervention rate. It is quick and easy to perform and causes few intraoperative complications. Impedance-controlled ablation offers the advantage of not requiring preoperative endometrial thinning. In addition, it can be performed at any time during the menstrual cycle, even during menstruation. The contraindications to this technique include an active genital or urinary tract infection and any anatomic abnormality, any condition or any intervention that can cause myometrial weakening, such as a previous classic cesarean section or transmural myomectomy. Furthermore, if the uterine cavity is less than 4 cm in length, the treatment will cause burning of the endocervical canal. It should be noted that the cervix has to be dilated to 8 mm in order to insert the device and that the dilatation process can be painful, even with local anesthesia.

6.2.6 Conditions relating to the innovative status of endometrial ablation techniques

Because they are innovative techniques, microwave ablation, hydrothermal ablation, cryoablation and impedance-controlled ablation should be reserved for certain hospitals with the necessary resources and expertise for systematically gathering and for analyzing all the data arising from their use and for disseminating these data to the medical and scientific communities. Randomized, controlled trials with a follow-up of at least three years after the initial ablation should be conducted to demonstrate the efficacy of these four second-generation techniques and to determine the long-term reintervention rate. As well, it would be useful to conduct other studies of these techniques to determine their cost-effectiveness and to confirm their safety when performed by a gynecologist who has not received special training (in the event that they are performed in clinics).

6.2.7 Endometrial laser intrauterine thermotherapy

Lastly, there are very few scientific reports on endometrial laser intrauterine thermotherapy, a second-generation technique not assessed in this report. As a result, there is little documentation on the efficacy and safety of this technique. Consequently, it is considered experimental (see Table 12). This new technique reportedly offers the advantage of being easy and very quick to perform and of being amenable to local anesthesia and narcosis. The above-mentioned conditions concerning the use of the other innovative techniques apply to endometrial laser intrauterine thermotherapy as well. Lastly, because of its experimental nature, this technique should be the subject of rigorous studies aimed at demonstrating its efficacy and safety and at

Table 12

Particular status of the various endometrial ablation techniques as per the Agency's terminology

Technique	**Status**
First-generation	
Transcervical resection	Accepted
Rollerball ablation	Accepted
Laser ablation	–[a]
Second-generation	
Thermal balloon ablation	Accepted
Microwave ablation	Innovative
Hydrothermal ablation	Innovative
Cryoablation	Innovative
Impedance-controlled ablation	Innovative
Endometrial laser intrauterine thermotherapy[b]	Experimental

[a] In Québec, laser endometrial ablation stopped being performed about ten years ago (according to a written communication from P.Y. Laberge, M.D., CHUQ Research Centre, November 2001).

[b] This technique is also known as Elitt™ (Endometrial Laser Intrauterine Thermal Therapy™).

determining the long-term satisfaction and reintervention rates and its cost-effectiveness. It would also be useful to conduct other studies to confirm its safety when performed by a gynecologist who has not received special training.

7

ECONOMIC ASPECTS OF ENDOMETRIAL ABLATION IN THE TREATMENT OF DYSFUNCTIONAL UTERINE BLEEDING

In the current scientific data on the economic evaluation of endometrial ablation, the terms "direct" and "indirect" are used to describe different types of costs. Direct costs are those incurred when setting up and conducting a health-care program, including the treatment of adverse events relating thereto. The recognition of these costs is often simply a list of the program's components, including the variable costs (hospitalization, medical consultations, drug utilization, medical supplies, etc.) and the fixed or general costs (electricity, heating, administration, capital expenditures, etc.). Furthermore, these costs include the personal expenses incurred by the patient and her immediate circle (transportation, lodging, child care, etc.). The indirect costs mainly concern the lost productivity due to the disease or treatment.

Performing nonabdominal hysterectomies could help reduce the cost differentials observed vis-à-vis the various endometrial ablation techniques. Vaginal and laparoscopic hysterectomies involve a shorter hospital stay than abdominal hysterectomies [Kovac et al., 1991; NHSCRD, 1995].

Furthermore, the more recent surgical techniques permit a shorter recovery and cause fewer complications than abdominal hysterectomy [Hidlebaugh, 2000; Lethaby et al., 2000d]. However, vaginal or laparoscopic hysterectomy is contraindicated in some women.

Researchers recently published the results of a retrospective analysis in which they compared the costs of hysterectomy as a function of whether it is performed abdominally, vaginally or laparoscopically, using the administrative database of Montréal's Royal Victoria Hospital [Abenhaim et al., 2001]. The study population consisted of women who had hysterectomies for benign conditions between April 1996 and November 1999. The hysterectomies were performed abdominally, vaginally and laparoscopically in 610, 297 and 21 of these women, respectively.

Laparoscopic hysterectomy and vaginal hysterectomy involve a significantly shorter mean hospital stay (2.2 and 4.2 days, respectively) than abdominal hysterectomy (4.9 days). Laparoscopic and vaginal hysterectomies entail higher theatre costs and lower nursing costs than abdominal hysterectomies. The total cost of hospitalization is considerably lower in the case of laparoscopic hysterectomy ($1,316.92 CDN) than abdominal ($1,993.32) or vaginal ($1,814.73) hysterectomy. It should be noted that the surgeon's fees and the hospital's overhead are not included in the total-cost calculation. The total cost of a laparoscopic hysterectomy might be influenced by the small number of women treated, a higher level of surgical experience, and the use of nondisposable instruments.

The results of an American study, too, indicate that the laparoscopic approach involves higher theatre costs and a shorter hospital stay than the abdominal approach [Simon et al., 1999]. The hospitalization costs for an abdominal hysterectomy are higher than for a laparoscopic hysterectomy because of the difference in the length of stay. According to a randomized, comparative trial, the direct costs of a laparoscopic hysterectomy are 1.7% higher than those of an abdominal hysterectomy [Ellstrom et al., 1998]. However, its indirect costs are 50.3% lower than those of an abdominal hysterectomy. The authors calculated that the total cost of a laparoscopic hysterectomy was 76.9% of that of an abdominal hysterectomy. The results of these studies corroborate those of the research carried out in Canada [Abenhaim et al., 2001].

7.1 Costs associated with the first-generation techniques

Although the results of controlled studies of hysterectomy and the first-generation endometrial ablation techniques have been published, very few of these studies were randomized or examined the economic repercussions of surgical treatment for dysfunctional uterine bleeding. A summary of the characteristics and results of the economic evaluations of endometrial ablation in the treatment of dysfunctional uterine bleeding is provided in Table G (see Appendix G).

The results of all the economic evaluations indicate that the first-generation ablation techniques involve fewer costs than hysterectomy (see Tables 13 and 14). It should be noted that almost all the economic analyses concerned the costs associated with surgical reinterventions and the treatment of intraoperative and postoperative complications. Only a few of these analyses examined the patients' personal expenses and lost wages due to the relatively long convalescence that a hysterectomy requires. Consequently, a direct comparison of these results cannot be made, since the methodology and outcome measures of interest vary from study to study.

According to a randomized, controlled trial of transcervical resection of the endometrium and abdominal hysterectomy, the hospitalization costs for a hysterectomy are three times higher than for a transcervical resection [Gannon et al., 1991]. The costs for a transcervical resection were lower than those for an abdominal hysterectomy because of the shorter hospital stays and theatre times. However, the cost of the additional procedures and the cost of treating the complications were not included in the economic analysis.

According to a prospective economic evaluation that ran parallel to a randomized, controlled trial [Dwyer et al., 1993] and that was based on the use of health-care system resources during the four months following the initial operation, the cost of a transcervical resection is lower than that of an abdominal hysterectomy [Sculpher et al., 1993]. On average, the total cost of a transcervical resection, including the cost of treating the complications and the cost of reintervention, was 47% lower than that of an abdominal hysterectomy. These results are corroborated by those of a second study, which examined health-related quality of life and costs two years after surgery [Sculpher et al., 1996]. The cost differential persisted over a long period of time but diminished. It was 29% after a mean follow-up of 2.2 years. To a large extent, the difference was due to the fact that a repeat resection or a hysterectomy was required in nearly one-fourth of the women initially treated by transcervical resection after randomization [Sculpher et al., 1996]. It should be noted that these costs do not include the resources used by the patient, her family or the community during the relatively long convalescence that hysterectomy requires.

Similar results were obtained in an economic evaluation carried out within the framework of a randomized, controlled trial [Pinion et al., 1994] of hysteroscopic endometrial ablation (by laser or transcervical resection) and hysterectomy (abdominal or vaginal) [Cameron et al., 1996; Grant et al., 1999]. The expenses incurred by the National Health Service (NHS) in the United Kingdom and by the patients during the 12 months following the initial operation were examined [Cameron et al., 1996]. In the case of hysteroscopic ablation for menorrhagia, the NHS's expenses were 24% (transcervical resection) or 20% (laser ablation) lower than for hysterectomy. On average, the personal expenses associated with hysteroscopic ablation were 71% lower than for hysterectomy. However, an economic analysis performed four years after the initial operation suggests that hysteroscopic ablation is no more economical than hysterectomy

Table 13

Results of prospective, comparative economic evaluations of the first-generation endometrial ablation techniques and hysterectomy

Study	Follow-up[a] (months)	Direct costs[b]		Indirect costs[b]	
		Endometrial ablation	Hysterectomy	Endometrial ablation	Hysterectomy
Gannon et al., 1991 United Kingdom	12[c]	£ 407[d,e]	£ 1,270[d,f]	No data	No data
Sculpher et al., 1993[g] United Kingdom Sculpher et al., 1996[g] United Kingdom	4 and 26.4[h]	After 4 months: £ 560.05[e] (± £ 261.22) After 26.4 months: £ 790 (± £ 49[illegible])	After 4 months: £1,059.73[f] (± £ 198.04) After 26.4 months: £ 1,110 (± £ 168)	No data	No data
Cameron et al., 1996[i] United Kingdom Grant et al., 1999[i] United Kingdom	12 and 48	After 12 months: Laser ablation £ 1,046 Transcervical resection £ 1,001 After 48 months: £ 1,231[j]	After 12 months: £ 1,315[k] After 48 months: £ 1,332	No data	No data

[a] Duration of follow-up after the initial operation.

[b] Costs per patient, including the cost of the additional interventions and the cost of treating the intraoperative and postoperative complications; mean value (± SD).

[c] Mean duration of follow-up (range: 9 to 16) for the endometrial ablation group. The duration of follow-up for the hysterectomy group is not given.

[d] The costs of the additional interventions and the treatment of the intraoperative and postoperative complications are not included.

[e] Transcervical resection.

[f] Abdominal approach.

[g] Efficacy data from a randomized, controlled trial [Dwyer et al., 1993].

[h] Equals 2.2 years.

[i] Efficacy data from a randomized, controlled trial [Pinion et al., 1994].

[j] By laser or transcervical resection.

[k] Abdominal or vaginal approach.

Table 14

Results of retrospective, comparative economic evaluations of the first-generation endometrial ablation techniques and hysterectomy

Study	Follow-up[a] (months)	Direct costs[b]		Indirect costs[b]	
		Endometrial ablation	Hysterectomy	Endometrial ablation	Hysterectomy
Brooks et al., 1994 United States	12	$3,749 US[c]	$6,412 US[d]	No data	No data
Brumsted et al., 1996 United States	45.4[e]	$5,159 US[f]	Abdominal approach: $8,833 US Vaginal approach: $8,132 US	At home[g]: $129 US At work: $315 US	Abdominal approach: At home[g]: $1,806 US At work: $4,410 US Vaginal approach: At home[g]: $1,204 US At work: $2,940 US
Ransom et al., 1996 United States	2	$3,765 US[h] ($2,822 to $7,011 US)	Abdominal approach: $9,736 US ($6,792 to $12,890 US) Vaginal approach: $7,413 US ($4,188 to $12,028 US)	No data	No data
Vilos et al., 1996[a] Canada	12	$2,174 CDN[f,i]	$4,231 CDN[i,j]	$105 CDN[i]	$1,142 CDN[i]
Hidlebaugh and Orr, 1998 United States	36	$5,434 US[h]	$8,417 US[k]	$525 US	$3,360 US
London et al., 1999 United States	12	$4,927.67 US[l] (± 2,900.85 US)	$9,231,15 US[l] (± $3,958.93 US)	No data	No data

[a] Duration of follow-up after the initial operation.

[b] Costs per patient, including the cost of the additional interventions and the cost of treating the intraoperative and postoperative complications; mean value (± SD) (range).

[c] By rollerball or transcervical resection.

[d] Abdominal or vaginal approach.

[e] Mean duration of follow-up (range: 19.1 to 78.7) for the endometrial ablation group. The duration of follow-up for the hysterectomy group is not given.

[f] By laser, rollerball or transcervical resection.

[g] Lost productivity of women at home and of those in the workforce.

[h] By rollerball.

[i] The costs associated with the intraoperative and postoperative complications were not included.

[j] Vaginal approach.

[k] Abdominal, vaginal or hysteroscopically assisted vaginal hysterectomy. A subgroup analysis showed the total direct and indirect costs to be $12,368, $9,256 and $13,365 US, respectively.

[l] Abdominal approach.

because of the high reintervention rate, although it did seem to be so one year after it was performed [Grant et al., 1999]. It was determined that, on average, the total cost of a hysteroscopic ablation was 93% of that of a hysterectomy four years after these procedures. The gradual decrease in costs corroborates the findings of Sculpher et al. [1996].

A cost-utility analysis of transcervical resection of the endometrium compared to abdominal hysterectomy was performed to assess cost-effectiveness [Sculpher et al., 1998a]. A randomized, controlled trial [Dwyer et al., 1993] and a follow-up study [Sculpher et al., 1996] were the main sources of data for the analysis. The decision analysis took into account the three main consequences of the surgical procedures: the increase in life expectancy, the qualitative aspects of a life thus prolonged, and the cost of the operation. The consequences of each procedure were expressed in quality-adjusted life-years (QALYs). In this model, the present value of the costs would be £794 in the women treated by transcervical resection and £1,139 in the women treated by abdominal hysterectomy two years after the initial operation. The present value of the QALYs was estimated at 1.363 in the women treated by transcervical resection and 1.593 in the women treated by abdominal hysterectomy. Thus, on average, abdominal hysterectomy would cost £345 more per patient than transcervical resection after two years of follow-up. However, it would increase the number of QALYs by 0.23. Consequently, for each additional QALY resulting from an abdominal hysterectomy the cost differential would be £1,500[14].

On the other hand, a sensitivity analysis indicates that the cost differential per additional QALY is highly sensitive to differences in hospitalization costs and the health score after the operation. The future increase in costs and benefits is a large area of uncertainty with regard to the cost-effectiveness of abdominal hysterectomy and transcervical resection. The decision analysis is based on data from a randomized, controlled trial with a 2-year follow-up [Sculpher et al., 1996]. The results obtained during the follow-up are therefore reasonably reliable. However, a prognosis made during subsequent years could change the economic balance between the two techniques [Sculpher et al., 1998a]. This factor highlights the importance of a long-term follow-up of participants in randomized, controlled trials of endometrial ablation and hysterectomy. Furthermore, Sculpher reports that it is more efficient to base the choice of treatment on the patient's preferences than to systematically perform the same type of procedure in every surgical candidate with dysfunctional uterine bleeding [Sculpher et al., 1998b].

Brooks et al. did a retrospective comparison of the costs associated with resectoscopic endometrial ablation (transcervical resection or rollerball ablation) and hysterectomy (abdominal or vaginal) in the treatment of dysfunctional uterine bleeding in women enrolled in a national managed health-care organization [Brooks et al., 1994]. They did not observe any difference between endometrial ablation and hysterectomy in terms of preoperative costs. However, endometrial ablation entails significantly lower perioperative costs. This difference is due mainly to the longer hospital stay required for hysterectomy. However, endometrial ablation involves significantly higher postoperative costs because of the reintervention rate. The total cost of resectoscopic endometrial ablation is lower than that of hysterectomy.

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[14] In Canada, a health program is considered efficient if the cost-effectiveness differential per QALY is less than $20,000 CDN [Laupacis et al., 1992].

Vilos et al. report that, in the treatment of menorrhagia, hysteroscopic endometrial ablation (by laser, rollerball or transcervical resection) costs on average of $3,094 CDN less than vaginal hysterectomy [Vilos et al., 1996a]. They included the costs associated with recovery and additional interventions but did not determine the cost of treating the intraoperative and postoperative complications. Furthermore, the duration of the postoperative follow-up was only 12 months.

Another economic evaluation compared hysteroscopic endometrial ablation (by laser, rollerball or transcervical resection) and abdominal or vaginal hysterectomy [Brumsted et al., 1996]. The determination of the direct costs covered the cost of the interventions performed after treatment failure. Endometrial ablation involved significantly fewer direct and indirect costs than abdominal or vaginal hysterectomy. The authors determined that the reintervention rate would have to be 53% in order for endometrial ablation to be less advantageous than abdominal hysterectomy from an economic standpoint. Unfortunately, the authors do not specify the duration of follow-up in the group treated by hysterectomy.

Another retrospective economic analysis examined the costs of three surgical procedures performed in the treatment of menorrhagia [Ransom et al., 1996]. Rollerball endometrial ablation, abdominal hysterectomy and vaginal hysterectomy were performed in the same number of patients. Rollerball ablation required a significantly shorter convalescence and entailed significantly lower hospitalization costs than the other two procedures. Vaginal hysterectomy involved lower hospitalization costs and a speedier return to work than abdominal hysterectomy. The authors of this analysis conclude that vaginal hysterectomy is considerably more efficient than abdominal hysterectomy as a definitive treatment for menorrhagia. The analysis did not examine the complications or long-term reintervention rate, since the follow-up after the initial operation lasted only two months.

As part of a case-control study, two American researchers did a long-term economic evaluation to compare rollerball endometrial ablation and hysterectomy in the treatment of menorrhagia [Hidlebaugh and Orr, 1998]. The hysterectomies had been performed abdominally, vaginally and vaginally with laparoscopic assistance in the same number of patients. The direct and indirect costs incurred during the three years following the initial operation were included, as were the costs associated with the additional operations performed in both groups. The operating time, length of hospital stay, recuperation time and postoperative complication rate were all significantly lower in the rollerball group than in the hysterectomy group. It follows that the direct and indirect costs of rollerball ablation are significantly lower than for hysterectomy. On average, the cost of rollerball ablation was $5,818 US less per case than hysterectomy.

Another economic analysis examined the potential economic benefits for third-party payers when hysteroscopic endometrial ablation (by laser, rollerball or transcervical resection) is chosen as an alternative to hysterectomy [London et al., 1999]. This retrospective evaluation of health-care claims included the total direct costs assumed by the third-party payer (reimbursement) and by the patient (copayment). The follow-up extended from the initial diagnosis to 12 months after the initial operation. The results indicate that average savings of about $4,300 US per case could be achieved by performing hysteroscopic endometrial ablation instead of abdominal hysterectomy to treat dysfunctional uterine bleeding.

Lastly, a single randomized, controlled trial examined the economic repercussions of the two endometrial ablation techniques that were investigated [Bhattacharya et al., 1997]. The investigators compared resource utilization for laser ablation and transcervical resection. They conducted a cost-minimization analysis after finding no marked difference between the two groups with regard to the clinical efficacy criteria. They assumed that the choice of repeat procedure depended on the surgeon's preferences rather than clinical need. They did not examine the use of health-care resources common to both ablation techniques. No difference between the two groups was observed with regard to the expenses incurred by the patient. Since it requires significantly longer theatre time and entails higher equipment costs, laser ablation involves an additional expense of £167 per patient [Hirsch, 1994].

7.2 Costs associated with the second-generation techniques

No controlled study of second-generation endometrial ablation techniques and first-generation techniques or hysterectomy in the treatment of dysfunctional uterine bleeding has examined the economic aspects of these procedures. When this report was being drafted, no economic evaluation of the second-generation techniques had been published.

Quantifying the economic repercussions of the new techniques is no easy task. The five second-generation techniques assessed in this report seem comparable to the first-generation techniques already performed in Québec in terms of efficacy, the level of satisfaction and the reoperation rate. However, the long-term efficacy and safety of repeat microwave ablation, hydrothermal ablation, cryoablation and impedance-controlled ablation are uncertain. From an economic standpoint, the potential benefits of the second-generation techniques include the fact that they take less time to perform and are associated with a lower incidence of intraoperative complications. However, the clinical significance of these two benefits has yet to be demonstrated.

All of the second-generation techniques involve relatively high purchase and utilization costs (single-use supplies). These costs and other direct costs associated with the surgical treatment of dysfunctional uterine bleeding in Québec are presented and commented on later in this report.

8

QUÉBEC CONTEXT

8.1 Surgical treatment of dysfunctional uterine bleeding in Québec

Statistics show that, in Québec, 12,147 women aged 35 and over underwent a hysterectomy in 1996-1997. The hysterectomy rate during that period was therefore 612 per 100,000 women in that age group. Dysfunctional uterine bleeding and dysmenorrhea (menstrual pain) were the main indication for 16.2% of the hysterectomies performed in Québec and the second leading reason for undergoing the procedure [Millar, 2001]. These figures do not differ significantly from those for all of Canada[15].

Most of the hysterectomies performed in Québec are performed abdominally, but the number and proportion of vaginal and laparoscopic hysterectomies are on the rise. Thus, the percentage of vaginal hysterectomies increased from 16 to 33% between 1981–1982 and 1996–1997. In 1996–1997, the mean length of hospital stay was 6 or 5.2 days for an abdominal and a vaginal hysterectomy, respectively. These figures differ significantly from those for all of Canada for the same period. The mean length of hospital stay for Canadian women who underwent an abdominal or vaginal hysterectomy was 5.1 and 4.1 days, respectively [Millar, 2001].

Endometrial ablation is a surgical procedure that is gaining in popularity. According to statistics from the Régie de l'assurance maladie du Québec (RAMQ), the number of Québec women of all ages (range: 15 to 84 years) treated by endometrial ablation increased sharply between 1995 and 1999, from 1,007 to 1,830 per year. This is an increase of nearly 82% in the frequency of this medical procedure during that period. In Québec, most endometrial ablations are performed in women aged 35 and older. It is interesting to note that the number and proportion of endometrial ablations in this age group is on the rise. Thus, the proportion of Québec women aged 35 and older when they underwent an endometrial ablation increased from 81.3% in 1995 to 87.8% in 1999.

The decision to perform a hysterectomy can depend on how physicians diagnose and practice and on their experience and opinions concerning the efficacy of this procedure. In turn, these factors can depend on how recently the physician was trained, as he or she is perhaps better informed about the other surgical procedures, and on the availability of the new treatments and of equipment in Québec hospitals. Thus, the presence of a university hospital in a given region can influence not only the attitude of the physicians affiliated with that hospital, but also that of all the physicians in the region [Millar, 2001].

Certain regional variations in the frequency of endometrial ablation observed in Québec may be due to whether or not the patients live in an urban setting. Given the distances, women with dysfunctional uterine bleeding who live in a rural area might find access to an alternative treatment more difficult. In borderline cases, the medical personnel and the patient herself might opt for a hysterectomy (in order to avoid the frequent trips required for a follow-up by a specialist) [Millar, 2001].

8.2 Economic repercussions of the second-generation techniques on Québec's health-care system

Data in the literature on the health benefits associated with a lasting decrease in menstrual blood loss do not presently enable us to perform a cost-benefit analysis of the second-generation techniques in the treatment of dysfunctional uterine bleeding.

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[15] See Section 3.2.

Based on published clinical data presented in this report, the second-generation techniques seem comparable to the first-generation techniques in terms of short-term efficacy, the level of satisfaction and the reintervention rate. They are reported to take less time and cause fewer intraoperative complications. However, the clinical and economic significance of these differences has yet to be demonstrated.

Nonetheless, the efficacy and especially the long-term reintervention rate should be assessed in rigorous studies. It would be very unwise to draw any firm conclusions about the costs associated with the second-generation techniques without having conducted a sufficiently long follow-up. Certain advantages of these new techniques could diminish if the long-term reintervention rates prove to be higher than the rates reported when this report was being drafted. Two researchers observed that the reintervention rate stabilized three years after the initial operation [O'Connor and Magos, 1996]. The economic evaluation should therefore include the direct and indirect costs incurred during a follow-up of at least three years in a comparison of the second-generation techniques and the first-generation techniques or hysterectomy.

Various costs directly associated with the endometrial ablation techniques approved in Canada and with hysterectomy are presented in Table 15. Unfortunately, this is but an incomplete picture because of insufficient data on the hospital costs associated with endometrial ablation, the costs resulting from intraoperative and postoperative complications or additional interventions, and the indirect costs of convalescence. For now, only the acquisition cost of the different apparatuses and single-use devices are directly quantifiable and can influence decision-making by managers in a more immediate fashion.

Table 15

Direct costs of the surgical treatment of dysfunctional uterine bleeding

Type of surgery	Direct costs in Québec (in Canadian dollars)				Surgeon's fees
	Cost of the device[a]	Utilization cost per treatment[a,b]	Pretreatment with endometrial thinning agents[c]	Hospital costs	
Hysterectomy (all approaches combined)	N/A[d]	N/A	Not necessary	2,369[e] (QC) 3,392[f] (ON) 2,352[g] (MAN)	330
First-generation techniques					
Laser ablation	No data	No data	47 to 382[h]	No data[i] (QC) 1,382[k] (ON) 969[l] (MAN)	180
Transcervical resection	2,145 to 3,472[j]	105[j]	47 to 382		180
Rollerball ablation	2,145 to 3,472[j]	105[j]	47 to 382		180

[a] This cost is negotiable and may be the subject of a special agreement between the hospital and the distributor or seller of the device (possibility of a free loan on the condition that a certain number of procedures are performed during a mutually agreed upon period of time). Nonetheless, these amounts give the reader an idea of the order of magnitude of the expenses involved.

[b] Single-use device.

[c] Pharmacist's fees not included. Estimation based on the RAMQ's formulary (April 2001). Depends on the agent used.

[d] N/A: Not applicable.

[e] Diagnostic-related groups (DRG) No. 358: Uterine and adnexa procedure for nonmalignancy; estimate; 1998-1999 data; mean length of hospital stay: 4.3 days.

[f] For comparison; case-mix group (CMG) No. 580: Uterine and adnexa procedure for nonmalignancy, without complications or comorbidity; actual value; 1995 dollars.

[g] For comparison; CMG No. 580; actual value; 1999 data; mean length of hospital stay: 4.4 days.

[h] Medroxyprogesterone acetate: $47; nafarelin: $280; danazol: $284; leuprolide acetate: $305; goserelin acetate: $382.

[i] No DRG evaluation for endometrial ablation.

[j] Cost figures provided by the company Karl Storz.

[k] For comparison; Day Procedure Group (DPG) No. 39: Uterine and adnexa procedure for nonmalignancy; actual value; 1995 dollars.

[l] For comparison; DPG No. 39; actual value; 1999 data.

Table 15 (Cont'd)

Type of surgery		Direct costs in Québec (in Canadian dollars)				Surgeon's fees
		Cost of the device[a]	Utilization cost per treatment[a,b]	Pretreatment with endometrial thinning agents[c]	Hospital costs	
Second-generation techniques[m]						
Microwave ablation	MEA	197,625[n]	625 to 700[o]	47 to 382[h]		150
Thermal balloon ablation						
	ThermaChoice II	10,000[p]	695	47 to 382		150
	Cavaterm plus	14,900	650	47 to 382	No data[i] (QC)	150
Hydrothermal ablation	Hydro ThermAblator	20,000 to 25,000[q]	550 to 600[r]	47 to 382		150
Cryoablation	Her Option	29,995 US	650 US	47 to 382	1,382[k] (ON)	150
Impedance-controlled ablation	NovaSure	25,000[s]	950	Not necessary	969[l] (MAN)	150
Endometrial laser intrauterine thermotherapy[t]	GyneLase	53,000[u]	495[v]	47 to 382		150

[a] This cost is negotiable and may be the subject of a special agreement between the hospital and the distributor or seller of the device (possibility of a free loan on the condition that a certain number of procedures are performed during a mutually agreed upon period of time). Nonetheless, these amounts give the reader an idea of the order of magnitude of the expenses involved.

[b] Single-use device.

[c] Pharmacist's fees not included. Estimation based on the RAMQ's formulary (April 2001). Depends on the agent used.

[h] Medroxyprogesterone acetate: $47; nafarelin: $280; danazol: $284; leuprolide acetate: $305; goserelin acetate: $382.

[i] No DRG evaluation for endometrial ablation.

[k] For comparison, DPG No. 39: Uterine and adnexa procedure for nonmalignancy; actual value; 1995 dollars.

[l] For comparison; DPG No. 39; actual value; 1999 data.

[m] Only the cost of the devices that had been approved by the HPFB as at July 31, 2002 are indicated here.

[n] Installation costs of $1,500 not included.

[o] Varies according to the number of cases treated per year: 0 to 50, $700; 51 to 100, $650; 101 or more, $625.

[p] Cost of $775 for the cables not included.

[q] Additional cost of $5,000 for an oscilloscope not included.

[r] Additional cost of $400 for using the heater canister 20 to 50 times not included.

[s] Additional cost of $200 for ten CO_2 cartridges (ten treatments per cartridge) not included.

[t] This technique is also known under the name of Elitt (Endometrial Laser Intrauterine Thermal Therapy).

[u] Including two fiber assemblies, ten single-use applicators and two pairs of anti-laser glasses.

[v] Additional cost of $2,500 for the fiber assembly (50 treatments per assembly) not included.

9

DISCUSSION

Dysfunctional uterine bleeding is the main indication for endometrial ablation. Endometrial ablation seems to be the surgical treatment of choice for this condition and should be preferred to hysterectomy. In fact, one of the basic principles in surgery is to remove (or destroy) only dysfunctional or diseased tissue and to preserve, as much as possible, the structural and functional integrity of the remaining healthy tissues [Garry, 1995a]. The cause of dysfunctional uterine bleeding is not clearly understood, but the endometrium is the organ from which the symptoms arise. Endometrial ablation permits control of uterine bleeding without the need to surgically remove most of the healthy uterus.

However, endometrial ablation does not guarantee amenorrhea, and a repeat ablation may be necessary after a few years. One randomized, controlled trial found the cumulative reintervention rate during the first four years after an initial endometrial duration to be 36%, with a 24% cumulative hysterectomy rate [Grant et al., 1999]. A published retrospective study conducted in Québec found the cumulative hysterectomy rate during the first five years after the initial operation to be 18.6% [Sylvestre et al., 2000]. In other words, about four women in five could avoid hysterectomy thanks to endometrial ablation. This could be considered progress in the treatment of medically refractory dysfunctional uterine bleeding.

Hysterectomy, which is considered the definitive treatment for dysfunctional uterine bleeding, causes considerably more morbidity than endometrial ablation. It is associated with a fairly high rate of morbidity and immediate and late complications, regardless of the surgical approach used. For instance, one published prospective study reports a morbidity rate of 42.8% and 24.5%, respectively, after abdominal and vaginal hysterectomy [Dicker et al., 1982]. Similarly, a retrospective survey found morbidity rates of 44.0% and 27.3%, respectively, after abdominal and vaginal hysterectomy [Varol et al., 2001]. A meta-analysis of the complications of laparoscopic hysterectomy found the morbidity rate to be 15.6% [Garry and Phillips, 1995]. Hysterectomy also carries a long-term risk of pelvic floor dysfunction, including colpoptosis and enterocele, with the result that genital prolapse can occur much later due to a loss of support. These complications lead to relatively high health-care costs and require other operations at a much later date[16].

Endometrial ablation is not a risk-free procedure, but its morbidity rate seems to be of a completely different magnitude. The MISTLETOE study reported overall intraoperative complication rates of 2.1 to 6.4%, depending on the hysteroscopic ablation technique used [Overton et al., 1997]. The results of a recently published study indicate that the probability of intraoperative complications is significantly greater during a repeat hysteroscopic endometrial ablation than the initial ablation (OR: 4.01; 95% CI: 1.63 to 9.87) [MacLean-Fraser et al., 2002]. For instance, uterine perforation is eight times more frequent during repeat ablations, probably because of the scars left by the first ablation.

Endometrial ablation and hysterectomy yield comparable satisfaction rates and a comparable improvement in various aspects of quality of life. According to certain published clinical trials, the level of satisfaction with endometrial ablation decreases with time, whereas the ability to engage in social activities, pain relief and overall health perceptions following hysterectomy continues to improve [Lethaby et al., 2000d].

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[16] Written communication from R. Sabbah, M.D., Hôpital du Sacré-Cœur de Montréal, December 2001.

Laparoscopic hysterectomy is the least expensive of all the hysterectomy approaches. Economic evaluations have shown that the direct costs of laparoscopic hysterectomy are higher than the cost of abdominal hysterectomy. However, this difference diminishes with surgical experience and the use of nondisposable devices. Laparoscopic hysterectomy involves considerably lower indirect costs than abdominal hysterectomy because, among other things, of the shorter convalescence that it requires [Hidlebaugh, 2000].

The first-generation endometrial ablation techniques involve lower direct and indirect costs than hysterectomy. However, the observed difference diminishes with time because of the relatively high reintervention rate [Grant et al., 1999; Phillips et al., 1998; Sculpher et al., 1996]. Comparing the cost-effectiveness of endometrial ablation techniques with that of hysterectomy is a complex task. Consequently, the simplistic conclusion that endometrial ablation is less expensive than hysterectomy and that the difference diminishes with time could very well arise from an inadequate economic evaluation [Lethaby et al., 2000d].

Endometrial ablation is an alternative to hysterectomy. However, the new, minimally invasive techniques will not result in hysterectomy being abandoned for the treatment of dysfunctional uterine bleeding. This is because, for women who wish to become amenorrheic, hysterectomy is presently the only surgical treatment that can guarantee such an outcome.

The availability of new techniques for treating dysfunctional uterine bleeding could lead women to seek surgery sooner than if hysterectomy were the only option available. After completing their childbearing, some women might even request an endometrial ablation–even if they have not been diagnosed with dysfunctional uterine bleeding–simply to avoid the inconvenience of normal menstruation. The increasing use of hormone replacement therapy in postmenopausal women is another factor promoting endometrial ablation, for hormone replacement therapy can lead to withdrawal bleeding or even cause some fibroids to become symptomatic. However, the number of women who will seek an endometrial ablation because of these effects cannot yet be determined. All of these situations could have significant economic repercussions on the health-care system.

Furthermore, adopting a technique as minimally invasive as endometrial ablation could lead to substantial changes in the hospital infrastructure. The second-generation techniques offer the advantage of being easy to perform and amenable to local anesthesia or narcosis. They would free up beds in ordinary treatment rooms but would require more day surgery facilities. Faster patient turnover could require additional hospital management costs. If a patient is discharged soon after the operation, it might be necessary to contact her the following day to see if there are any complications. Eventually, the new endometrial ablation techniques might be performed at a clinic affiliated with a hospital or at a private clinic without hospitalization.

One must know not only what the direct and indirect costs of the surgical procedures are, but also, the immediate and long-term costs and benefits, the reintervention rate and the satisfaction rate with the treatment in order to do a proper cost-effectiveness comparison of endometrial ablation and hysterectomy in the treatment of dysfunctional uterine bleeding. The costs and the perceived economic benefits of the new techniques will be of interest to hospital and public administrators and will have major repercussions on the diffusion of these new, minimally invasive procedures.

Thus far, we have presented the arguments from the perspective of the surgeon and health-care system. But the most powerful argument in favour of endometrial ablation comes from women who are bothered by dysfunctional uterine bleeding. Many of these women simply do not want to lose their uterus, especially if it is normal in structure. If given the option, many will choose to keep their uterus. Most women with dysfunctional uterine bleeding do not request a hysterectomy or even amenorrhea but seek, above all, relief from this bothersome symptom [Garry, 1995a].

Medical treatment is seldom a lasting solution and is not without adverse effects. If the patient wishes to keep her uterus, consideration might be given to endometrial ablation as an alternative to long-term drug therapy [Nagele et al., 1998]. The new costs associated with endometrial ablation should therefore be weighed against potential drug savings. The changes that can affect the quality of life and productivity of patients who abandon medical treatment for endometrial ablation should be taken into account as well.

The patient's or employer's perspective on the cost of the new surgical techniques is most likely different. All endometrial ablation techniques cause less postoperative pain and involve a speedier recovery. Shortening the convalescence by three to four weeks is beneficial to the patient, employers and the community. The patient's family and the community thus avoid having to care for the patient at home and to look after young children for an extended period of time. Since the employee returns to work much sooner, it costs the employer less in terms of lost productivity or of hiring temporary personnel. Arrangements for taking care of housework are thus necessary for only a short period of time. The patient and the family members who look after her have more free time and therefore a better quality of life. In addition, the patient has fewer travel expenses in connection with the postoperative follow-up. Although all of these costs are difficult to quantify, these minimally invasive techniques offer definite benefits from a societal perspective.

Nagele et al. conducted an observational study based on postal questionnaires to determine why menorrhagic women had chosen endometrial ablation instead of hysterectomy. The mean duration of follow-up was 45 months [Nagele et al., 1998]. Of the 106 randomly selected women who had been treated by endometrial ablation and who answered the questionnaire, 98 (92.4%) were satisfied or very satisfied with the treatment. More than half the women indicated that they would find endometrial ablation acceptable even if there was no chance of amenorrhea, if the probability of a lighter menstrual flow was greater than or equal to 40%, if the likelihood of dysmenorrhea decreasing was greater than or equal to 30%, if the risk of requiring a repeat ablation or a hysterectomy was less than or equal to 25% and if the risk of uterine cancer after surgery was 1 in 200 or less. For these women, the three most important advantages of endometrial ablation over hysterectomy were the avoidance of major surgery, the speedy return to normal activities, and the short hospital stay.

These results raise two points. First, it seems likely that most women who request an endometrial ablation because of dysfunctional uterine bleeding constitute a population different from those who opt for a hysterectomy. Amenorrhea is not an important treatment outcome for these women. In fact, endometrial ablation is considered more of an alternative to long-term drug therapy and offers the additional advantage of delaying or even avoiding a hysterectomy. Consequently, if a hysterectomy is performed at a later date, the initial surgical treatment is not necessary considered to have failed [Nagele et al., 1998].

Second, if women treated by endometrial ablation are different from those who undergo a hysterectomy, the decrease in the hysterectomy rate for dysfunctional uterine bleeding could not have been as large as expected when the new techniques became available [Nagele et al., 1998]. Bridgman reports that the proportion of women with dysfunctional uterine bleeding treated by endometrial ablation increased from 0 to 30% between 1988 and 1993 in the Mersey region in the United Kingdom [Bridgman, 1994]. However, very little change was observed in the hysterectomy rate during that period. This suggests that endometrial ablation has not replaced hysterectomy in the treatment of dysfunctional uterine bleeding but is rather an additional alternative, a less radical surgical treatment that some women might prefer [Bridgman, 1994; Kammerer-Doak and Rogers, 2000; Weber, 2000].

The results of a 4-month, randomized, controlled trial indicate that medical treatment is less effective than transcervical resection of the endometrium [Cooper et al., 1997]. The satisfaction rate was considerably higher after transcervical resection than after medical treatment (76% and 27%, respectively; $P < 0.001$). In addition, the proportion of women who considered the treatment acceptable was higher in the transcervical resection group than in the drug therapy group (93% and 36%, respectively; $P < 0.001$). Although medical treatment led to a significant reduction in dysmenorrhea and menstrual blood loss, these reductions were modest compared to those resulting from transcervical resection ($P < 0.001$). The 2-year follow-up of the participants treated in this study also showed transcervical resection to be more effective than medical treatment [Cooper et al., 1999b]. Once again, the satisfaction and treatment acceptability rates were significantly higher in the women treated by transcervical resection than in those who received medical treatment. Nearly 6 women in 10 in the medical treatment arm required surgery (endometrial ablation, hysterectomy or both) during the two years following the initial treatment. During the same period, 17% of the women treated by transcervical resection required repeat surgery.

The new levonorgestrel IUD (Mirena) could prove to be both an effective contraceptive and a lasting form of treatment for dysfunctional uterine bleeding, constituting an alternative to surgery for this condition. Some studies show that between 64 and 80% of hysterectomy candidates on a waiting list cancel their surgery within six months of being fitted with a levonorgestrel IUD [Luukkainen, 2000; Prentice, 1999]. In randomized, controlled, single-centre trials, it was observed that using this IUD led to a significant reduction in menstrual blood loss in most cases, but that the reduction was significantly smaller than after transcervical resection [Crosignani et al., 1997b; Istre and Trolle, 2001]. Nonetheless, large, randomized trials should be conducted to properly compare the levonorgestrel IUD and endometrial ablation from the standpoint of efficacy.

It seems difficult to do a direct comparison of the results of studies of endometrial ablation techniques for dysfunctional uterine bleeding because the study populations, methodology and outcome measures vary from study to study. Furthermore, the actual and perceived severity of the symptoms (blood loss of 80 mL or more per cycle), the women's ages and expectations, the presence of a uterine disease causing bleeding, the intrinsic efficacy of the surgical procedure, the surgeon's skill, and the uterine healing process are all factors that can influence endometrial ablation outcomes.

There are substantial differences between the studies in terms of their design, their inclusion and exclusion criteria, or even the methods for evaluating menstrual blood loss, quality of life or satisfaction with the surgical treatment. Although data from long-term, nonrandomized studies are reliable, one has to settle for usually short follow-ups in the case of randomized, controlled trials. Menstrual blood loss and dysmenorrhea can increase with time after an endometrial ablation [NHSCRD, 1995]. The efficacy and the reintervention rates reported in published studies therefore depend on the duration of follow-up [Lethaby et al., 2000d].

Some studies have examined endometrial ablation preceded by endometrial thinning, while others have not. Endometrial thinning with pharmacological agents might not lead to any improvement in clinical criteria or in the satisfaction of patients treated by transcervical resection or thermal balloon ablation (ThermaChoice) [Kriplani et al., 2002; Lissak et al., 1999; Rai et al., 2000]. Patients could thus be spared a potentially expensive preoperative medical treatment that can sometimes have adverse effects. Despite the fact that no improvement in clinical criteria or in patient satisfaction was observed in three clinical trials, another study reports the benefits offered by preoperative endometrial thinning, including less fluid absorption and less surgical time, plus better operating conditions [Kriplani et al., 2002]. Furthermore, it is not always convenient to schedule an endometrial ablation during the proliferative phase of the menstrual cycle, not only because of the unpredictability of each women's cycle, but also because an admission date has to be set several weeks in advance. Consequently, endometrial thinning with pharmacological agents might be useful in a candidate for either of these ablation techniques, for it makes it easier to plan the operation. Endometrial thinning by curettage can also be useful, regardless of the ablation technique to be used, and can be performed in lieu of administering pharmacological agents.

Prospectively documenting menstrual blood loss using a validated pictorial chart method [Higham et al., 1990; Janssen et al., 1995] is now a basic feature of recent clinical studies of the treatment of dysfunctional uterine bleeding [Corson, 2001; FDA, 1997; FDA, 2001b; FDA, 2001d; Heppard et al., 2001; Meyer et al., 1998]. A diary score of 100 gives a sensitivity of 86% and a specificity of 81% with regard to actual menstrual blood loss of at least 80 mL and is indicative of clinical menorrhagia [Higham et al., 1990]. Women with a score of 150 are therefore menorrhagic (inclusion criterion). Treatment success is based on a reduction in scores of at least 150 before treatment to 75 or less one year after the initial intervention. The use of such methods to evaluate blood loss improves study population homogeneity and permits interstudy comparisons.

Patient withdrawals are frequent in long-term studies of endometrial ablation techniques for the treatment of dysfunctional uterine bleeding. For example, a long-term clinical study that compared thermal balloon ablation (ThermaChoice) and rollerball ablation reported dropout rates of 13.1% and 22.2% after 12 and 36 months of follow-up, respectively [Loffer, 2001; Meyer et al., 1998]. In such circumstances, special efforts should be made to gather data on dropouts when their condition would have been evaluated had they remained until the end. These data would contribute to a better evaluation of the bias caused by the dropout rate on the evaluation of the therapeutic effect and would help determine the effect of such bias on interpreting results [Cucherat, 1997]. In the case of studies where the analysis was by intention-to-treat, a high dropout rate can result in a reduction of any effect that might be observed. On the other hand, a per-protocol analysis can be distorted by overevaluating the effect, because of the number of dropouts. Since most of the studies did not present the results of the intention-to-treat analysis and since the analyses concerned only those subjects who had participated in the trial up to the end, the results could be biased.

The first-generation endometrial ablation techniques seem comparable in terms of efficacy and the reintervention rate. Also, the laser- and rollerball-based techniques seem to cause fewer intraoperative complications than transcervical resection [Overton et al., 1997]. Furthermore, rollerball ablation is especially indicated for uterine bleeding due to anticoagulant therapy.

The five second-generation techniques assessed in this report seem comparable to the first-generation techniques already performed in Québec in terms of efficacy, the level of satisfaction and the reoperation rate. However, although microwave ablation, hydrothermal ablation, cryoablation and impedance-controlled ablation seem to be safe and effective procedures for treating dysfunctional uterine bleeding, we do not have any data on their long-term efficacy from large, randomized, controlled trials. The new techniques are quick and easy to perform. They can also be performed with local anesthesia (with or without prior intravenous sedation) or under narcosis. However, they involve relatively high purchase and utilization costs (single-use supplies).

The second-generation endometrial ablation techniques are expected to cause few problems. However, they do carry a risk of complications, including hematometra, infection and injury to internal organs. As with any other technique performed blind, the main concern with the second-generation ablation techniques is the risk of an accidental perforation and of subsequent bowel injury. Given that all of these new techniques are performed without visual hysteroscopic monitoring (with the exception of hydrothermal ablation), the physician should make a diagnosis based on a visual examination prior to treatment, as well as a diagnosis supported by a pathophysiological study which includes a hysteroscopy and, at the very least, an endometrial biopsy. It is also advisable to perform a hysteroscopy after the treatment to check that only the uterine cavity was treated [Vilos et al., 2001].

A recently published systematic review compared the second-generation endometrial ablation techniques with the first-generation techniques in the treatment of uterine bleeding [Lethaby and Hickey, 2002]. A systematic search in the computerized literature databases was conducted up to September 2001. In all, four second-generation ablation techniques were evaluated, namely, microwave ablation, thermal balloon ablation, hydrothermal ablation and intrauterine electroballoon ablation (Vesta). The review revealed the immediate advantages of the second-generation ablation techniques over the first-generation techniques. The second-generation techniques take less time to perform (weighted mean difference [WMD] of −11 minutes; 95% CI: −18.6 to −2.6) and are more likely to be performed with local anesthesia (OR: 7.6; 95% CI: 1.1 to 52.7). The second-generation techniques result in significant but comparable reductions in menstrual blood loss. No difference was found between the first- and second-generation techniques in terms of the level of satisfaction, the complication rate, the need for further treatment or the inability to work.

There are differences between Lethaby and Hickey's systematic review and ours. First, our search in the computerized literature databases was done up to July 31, 2002, i.e., for an additional 11 months, with the result that we were able to include recent data on two new techniques, cryoablation and impedance-controlled ablation. Furthermore, we excluded the studies of intrauterine electroballoon ablation, since this technique had been abandoned. Despite these differences the results are concordant.

10

CONCLUSION

Medical treatment is seldom a lasting solution to dysfunctional uterine bleeding and is not without adverse effects. Uterine curettage will stabilize bleeding in some women, but its effects are almost never lasting. Although it is a definitive treatment, hysterectomy carries substantial surgical risk, with considerable drawbacks and costs.

Endometrial ablation has been proposed, since it is a less invasive technique, more convenient and less expensive when no other gynecological condition is involved. However, the treatment outcomes are not always as clearly predictable as those of hysterectomy. Women with dysfunctional uterine bleeding prefer endometrial ablation to hysterectomy because it enables them to avoid major surgery and permits a shorter hospital stay and a shorter convalescence. Hysterectomy can cause many psychological and physical changes in a woman. Nonetheless, it continues to offer a high level of satisfaction because it guarantees the cessation of bleeding.

Various energy sources have been used to destroy the endometrium, and all seem comparable in terms of efficacy and the reintervention rate. Since hysteroscopic endometrial ablation (by laser, rollerball or transcervical resection) and thermal balloon ablation have accepted status, there would be no particular conditions governing their use.

On the other hand, because they are innovative techniques, microwave endometrial ablation, hydrothermal endometrial ablation, endometrial cryoablation and impedance-controlled endometrial ablation should be reserved for certain hospitals with the necessary resources and expertise for systematically gathering and for analyzing all the data arising from their use and for disseminating these data to the medical and scientific communities. Randomized, controlled trials with a follow-up of at least three years after the initial ablation should be conducted to demonstrate the efficacy of these second-generation techniques and to determine the long-term reintervention rate. It would also be useful to continue investigating these techniques to determine their cost-effectiveness and to confirm their safety when performed by a gynecologist who has not received special training (in the event that they are performed in clinics).

Lastly, because of its experimental nature, endometrial laser intrauterine thermotherapy, a second-generation technique not assessed in this report, should be the subject of rigorous studies aimed at demonstrating its short-and long-term efficacy and safety and at determining its cost-effectiveness and reoperation rate. Also, the use of this technique should be governed by the conditions that apply to innovative techniques.

Technologically, endometrial ablation is evolving at an extremely rapid pace, with randomized, controlled trials of the second-generation techniques presently underway or recently completed. The results of these clinical trials should be published within 12 to 24 months. These rapid changes require instituting a monitoring process and periodically publishing updates, which would enable one to reassess the specific status of each endometrial ablation technique.

In conclusion, we often observe a gap between clinical practice and evidence-based evaluative research. The incidence of surgical complications, the ease of use, and personal clinical experience clearly contribute to forming an opinion of the clinical utility and efficacy of any treatment. Improvements to and the rapid diffusion of new techniques facilitate their adoption by clinicians, even in the absence of published scientific data.

10.1 Repercussions on the practice of medicine and on public health

Women's expectations and preferences seem to be important determining factors for the best type of surgical treatment for dysfunctional uterine bleeding. The patient should be properly informed of the likely benefits and risks of hysterectomy and endometrial ablation. A well-informed woman will be able to choose the surgical treatment she considers the most appropriate herself.

Since the second-generation endometrial ablation techniques require less surgical skill and experience, we should observe an increase in the number of gynecologists offering this therapeutic option and, consequently, greater access to these techniques by Québec women. Steps will necessarily have to be taken to ensure that surgeons have not only the technical skills, but also the training needed to carefully select candidates for this type of treatment. This is because a good knowledge of the indications and contraindications has a direct impact on the level of satisfaction with the treatment and on the failure and reoperation rates.

A woman with dysfunctional uterine bleeding who wishes to undergo an endometrial ablation should have completed her family. A woman of reproductive age who is sexually active should subsequently use contraception, since she can become pregnant after the ablation. In postmenopausal women, the effects of hormone replacement therapy on residual endometrium are unknown. Any woman whose endometrium has been ablated and who is on hormone replacement therapy should receive an estrogen-progestin combination. It is possible for cancer to develop in residual endometrium after an ablation, and such cancer can be difficult to diagnose because of the scar tissue that forms in the uterine cavity. This is why one should evaluate the status of any woman with suspicious symptoms after an endometrial ablation.

The availability of the new techniques for treating dysfunctional uterine bleeding could lead women to seek surgery sooner than if hysterectomy were the only procedure available. Milder cases, which are normally treated by more conservative methods, could undergo less invasive treatment and experience an easier convalescence with endometrial ablation. The overall frequency of surgery could increase as a result because of the lower threshold for treating dysfunctional uterine bleeding. However, this increase should be offset by the decrease in the use of long-term drug therapy, although such therapy is not always effective and sometimes causes adverse effects. Endometrial ablation could therefore improve these patients' quality of life.

Some women with serious medical conditions who would not tolerate general anesthesia and intra-abdominal surgery could have their problem, otherwise potentially life-threatening, taken care of with the new techniques.

Unlike hysterectomy, endometrial ablation does not guarantee the cessation of menstrual flow and may require reoperation during the years following the initial procedure. The new endometrial ablation techniques involve relatively high equipment purchase and utilization costs. Furthermore, adopting a technique as minimally invasive as endometrial ablation could lead to substantial changes in the hospital infrastructure.

The patient's perspective on the cost of the new surgical procedures could very well be different. All the endometrial ablation techniques involve less postoperative pain and are characterized by a speedier recovery. Endometrial ablation could offer benefits for women's health, thanks to the lasting decrease in menstrual blood loss.

For all of these reasons, the repercussions of endometrial ablation techniques and, consequently, their role in the treatment of dysfunctional uterine bleeding can be fully defined only after a long-term follow-up.

10.2 Consequences on research

Endometrial ablation techniques and the latest hysterectomy procedures (vaginal and laparoscopic) should be compared in randomized trials. It seems that the latest hysterectomy techniques permit a shorter convalescence and cause fewer complications than abdominal hysterectomy. As well, longer-term studies should be conducted to properly determine the cost differentials between the two types of surgery and the reintervention rates associated with the various endometrial ablation techniques.

The endometrial ablation techniques should be compared with each other in randomized trials in order to determine which one is the most effective, the safest and the least expensive alternative to hysterectomy. It should also be determined if the second-generation endometrial ablation techniques are as effective as the first-generation techniques, especially for the treatment of fibroids.

In addition, controlled studies should be conducted to examine the effectiveness and cost-effectiveness of the more promising surgical procedures in terms of quality of life and acceptability. Lastly, endometrial ablation might be considered an alternative to long-term drug therapy. One should therefore examine the consequences of this shift in treatment strategy on patient quality of life and productivity and its economic repercussions.

APPENDICES

APPENDIX A
Status of medical technologies based on AETMIS' classification

The Agency developed the following classification for determining the status of the technologies that it assesses [CETS, 1998].

A.1 Experimental status

" The term *experimental* will be used here to describe a procedure whose effectiveness has yet to be established. Such a procedure should therefore not be used in health-care facilities, except in the context of research projects."

A.2 Innovative status

" The term *innovative* will be used to describe a technology which has passed the experimental stage and whose effectiveness has been established. However, because of a lack of experience, certain indications for its use and various aspects of its application are not yet clearly defined. To gain further knowledge of such technology, it would be important to gather systematically all the information acquired from its utilization and to communicate it to the medical community in the form of a clinical research report or systematic review or to an appropriate registry. To further these objectives and to prevent its premature widespread use, such technology should be restricted to certain authorized university hospitals which have the necessary resources and knowledge."

A.3 Accepted status

"The term *accepted* will describe a well-established technology for which there is a long history of use and knowledge of, or failing that, universal acceptance of, its effectiveness in all its applications."

APPENDIX B

Description of endometrial ablation techniques

B.1 Laser endometrial ablation

This technique consists in destroying the endometrium by photocautery using a neodymium:yttrium-aluminum-garnet (Nd:YAG) laser device.

Irrigation fluid, usually normal saline, is delivered into the uterus until an intrauterine pressure of up to 80 to 100 mm Hg is obtained. The volume of fluid delivered is measured in order to avoid fluid overload. After the hysteroscope is inserted, the physician visually examines the endometrium. The laser device is slid through the operating channel of the hysteroscope, then activated at a power level of approximately 50 to 80 W. A beam is then emitted by a quartz fiber with a diameter of 600 µm [HTAC, 2000; Kammerer-Doak and Rogers, 2000; Ke, 1997].

There are two laser endometrial ablation techniques, "touch" and "nontouch". In the touch technique, the tip of the laser fiber is lightly applied to the endometrial surface and gently swept across the uterine cavity. In the nontouch technique, the laser tip is kept within 1 to 5 mm of the endometrial surface but never touches it, and the beam sweeps the uterine wall at a perpendicular angle [HTAC, 2000; Kammerer-Doak and Rogers, 2000; Ke, 1997]. Ablating at a perpendicular angle reduces beam reflection and increases tissue absorption. The ablation is completed faster in this manner [Kammerer-Doak and Rogers, 2000]. However, it is difficult to keep the laser perpendicular to the wall of the isthmus and to distinguish between those parts of the endometrium that have been exposed to the laser (excised) and those that have not. The results yielded by the nontouch technique are therefore inferior to those yielded by the touch technique [Kammerer-Doak and Rogers, 2000].

Laser ablation begins at the cornual and fundal areas with the delivery of short, 5- to 10-second bursts of thermal energy. The anterior wall is ablated to the level of the cervical os, followed by ablation of the lateral and posterior walls. The Nd:YAG laser coagulates and denatures the endometrium to a depth of about 4 to 6 mm [HTAC, 2000; Kammerer-Doak and Rogers, 2000; Ke, 1997]. As coagulation proceeds, tissue damage is minimized, since the energy absorbed decreases and the amount that is reflected increases. Laser ablation takes approximately 20 to 35 minutes [HTAC, 2000; Ke, 1997].

B.2 Transcervical resection of the endometrium

This technique involves electrocautery of the endometrium using a resectoscope at whose tip is a metal loop supplied with high-frequency electrical current.

The goal of transcervical resection is to burn the basement layer of the endometrium and the first few millimetres of the myometrium. The size of the metal loop varies from 4 to 8 mm. The largest loop removes approximately 4 mm of endometrial tissue and 2 to 3 mm of myometrium. However, its use requires greater surgical skill because of the risk of uterine perforation. The 4-mm loop removes approximately 2 mm of tissue. While the use of this loop carries a smaller risk of perforation, it requires several passages and therefore takes more time. Consequently, there is a greater risk of fluid overload [Holt and Gillmer, 1995; Kammerer-Doak and Rogers, 2000].

Resection begins at the fundal area and continues toward the isthmus up to the internal cervical os. Since it can be difficult to reach the cornual regions with the wire loop, a rollerball electrode may be used to destroy that part of the endometrium by electrocoagulation. Using mixed current (cutting and coagulating) of 80 to 120 W minimizes the risk of perforation and maximizes endometrial destruction. Pieces of resected tissue may be removed by curettage or with polyps forceps [Garry, 1995b; HTAC, 2000; Holt and Gillmer, 1995; Kammerer-Doak and Rogers, 2000; Ke, 1997]. Transcervical resection takes 15 to 20 minutes [Garry, 1995b; HTAC, 2000; Ke, 1997].

B.3 Rollerball endometrial ablation

From a technical standpoint, rollerball endometrial ablation is similar to transcervical resection. It is a type of endometrial electrocoagulation performed with a resectoscope at whose tip is a spherically shaped piece of metal (rollerball) supplied with high-frequency electrical current.

During rollerball ablation, a rollerball electrode measuring 2 to 4 mm in diameter is rolled over the surface of the endometrium at a speed of 10 to 15 mm per second. The basement layer is destroyed to a depth of 3 to 4 mm by electrocoagulation [Garry, 1995b; HTAC, 2000; Ke, 1997; Valle, 1995]. The electrocoagulation starts at the fundal area and continues toward the isthmus up to the internal cervical os. The type and fine adjusting of the electrical current can vary. The rollerball electrode can be activated only when it is in contact with tissue. The risk of complications due to an ill-timed discharge is therefore lower [Kammerer-Doak and Rogers, 2000; Valle, 1995]. Rollerball ablation takes about 15 to 30 minutes [Valle, 1995].

Although most authors suggest rolling the electrode twice over the endometrial surface, there are no published long-term results of comparisons of single- and double-pass rollerball ablation [Kammerer-Doak and Rogers, 2000].

B.4 Microwave endometrial ablation

As with all other forms of electromagnetic energy, microwaves penetrate biological tissues to a depth that depends on the electrical properties of the tissue and the frequency of the electromagnetic waves [Hodgson et al., 1999; Sharp et al., 1998; Sharp et al., 2000]. The penetration of microwaves decreases as their frequency increases. The frequency of the waves admitted by microwave ovens varies from 2.3 to 2.5 GHz. At such frequencies, the depth of penetration of electromagnetic waves in tissues with a high water content is about 18 mm. At this depth, the wave amplitude is no longer but 10% of the amplitude at the surface of the tissue. As a result, heating of tissues is negligible beyond this point [Hodgson et al., 1999; Sharp et al., 1998; Sharp et al., 2000].

Microwave Endometrial Ablation System

The MEA operates at a frequency of 9.2 GHz. At this frequency, the microwaves are almost totally absorbed by endometrial tissue to a depth of close to 3 mm. Beyond this depth, electromagnetic energy is negligible, and the microwaves do not reach the myometrium or escape from the uterus [Hodgson et al., 1999; Sharp et al., 1998; Sharp et al., 2000].

Since the circular waveguide is filled with a material whose dielectric constant is greater than that of air, the length of the radiating microwaves is very effectively reduced. Thanks to this material, the manufacturer was able to reduce the diameter of the waveguide to 8 mm [Hodgson et al., 1999; Sharp et al., 1998; Sharp et al., 2000]. The tip of the waveguide has been designed in such a way as to heat tissue in a hemispherical pattern so as to effectively radiate electromagnetic energy in the uterine cavity. Since the microwaves propagate effectively at the surface of the tip, tissue cohesion is better reduced at a far distance from the tip [Sharp et al., 1998]. The total depth of necrosis depends on the power of the microwaves emitted and on the length of exposure. Thanks to data from experimental trials, one can obtain an in vivo depth of necrosis of 5 to 6 mm [Sharp et al., 1998; Sharp et al., 2000].

The MEA includes a control unit mounted on a dedicated cart, a printer, a coaxial cable (for electromagnetic energy), a signaling cable and a set of applicators (waveguides). The central unit includes a microwave generator and a monitoring device, both enclosed in the same housing. A keypad is used to enter clinical data and serves as a control panel. The software that comes with the device controls the microwave generator, the applicator's characteristics and the treatment parameters.

The applicator is a consumable device with a programmed operating lifespan of 30 treatments. Each use of the applicator is recorded on an electronic chip in the applicator. The applicator is returned to the company (Microsulis) after 30 uses or one year of service.

The safety devices include alarm messages and a locking mechanism that actuate in the unlikely event of a malfunction of the system or applicator, or of operator error. A safety locking device prevents activation of the generator as long as the temperature has not reached at least 30°C in the applicator thermocouple and as long as the applicator per se is not in contact with endometrial tissue. The applicator handle contains a thermocouple as well. Temperature is controlled in the tip and handle by means of alarm and shut-off devices [Sharp et al., 1998].

Description of the technique

Microwave ablation can be performed with general or local anesthesia or under narcosis [Bain et al., 2001]. Before the operation, the characteristics of the uterine cavity can be checked by hysterosonography or by CO_2 hysteroscopy. Glycine hysteroscopy is ill-advised before microwave ablation because of the possibility of the solution hindering the effect of the microwaves on the endometrium [Tulandi and Felemban, 2001]. The physician starts by measuring the uterine cavity with a centimeter hysterometer, then dilates the cervix to 9 mm with a Hegar dilator. Next, the applicator is inserted until its tip touches the uterine fundus. The centimeter graduations on the applicator are used to check that the depth of insertion is indeed the length of the uterine cavity as determined by hysterometry [Hodgson et al., 1999; Sharp et al., 1998; Tulandi and Felemban, 2001].

After the customary checks of the device, the applicator is supplied, by means of a pedal, with 30-W electromagnetic power from a generator. Because of loss in the applicator, the exit power is about 22 W. A thermocouple in the applicator tip records a temperature proportional to the temperature of the microwave-heated tissue. The temperature of the tissue increases quickly and is displayed on the device monitor. The displayed temperature is slightly lower than the actual temperature of the tissue [Hodgson et al., 1999; Sharp et al., 1995; Sharp et al., 1998; Sharp et al., 2000].

During the initial increase in temperature, the tip of the applicator is moved over the uterine fundus in a lateral to-and-fro motion to ensure that the fundus is heated uniformly and that the cornual regions are treated in their entirety. By keeping the measured temperature within a therapeutic range (between 70 and 80°C) that can be verified on the monitor, the surgeon can deliver the desired energy dose to the endometrium in a uniform manner. Once the fundus has been treated, the surgeon slowly removes the applicator while continuing to sweep the surface of the uterine cavity and keeping the temperature within the therapeutic range as much as possible [Hodgson et al., 1999; Sharp et al., 1998; Tulandi, 1999]. The untreated surfaces can be recognized by their lower temperature. The applicator is brought to a standstill on the untreated surface until the desired temperature is achieved, after which the to-and-fro motion is resumed. In this manner, the entire uterine cavity is treated while the applicator is gradually removed. The appearance of a 35-mm black strip printed under the applicator tip tells the surgeon that the activated tip has reached the internal cervical os. Interrupting the current as soon as the strip becomes visible avoids heating the external cervical os. The applicator is then removed [Hodgson et al., 1999; Sharp et al., 1998].

On average, treating a normal-size uterus (75 to 85 mm in length) takes less than three minutes. It takes six or seven minutes to treat a large uterus (100 to 110 mm) and less than two minutes to treat a small one (60 to 70 mm) [Sharp et al., 2000].

B.5 Thermal balloon endometrial ablation

There are three thermal balloon systems, the ThermaChoice II, the Cavaterm plus and the MenoTreat. Each includes a handset equipped with a single-use balloon catheter and a controller. The controller regulates the intrauterine pressure, balloon temperature, fluid circulation and treatment time [Brun et al., 2000; Hawe et al., 1999; Ulmsten et al., 2001].

ThermaChoice Uterine Balloon Therapy System

Originally, the balloon was made of latex. Improvements have since been made to the device. The ThermaChoice II now includes a new silicone balloon and a fluid mixing element housed inside the catheter that circulates lukewarm fluid and ensures constant temperatures throughout the treatment. The catheter is 16 cm in length and 4.5 mm in diameter.

After anesthesia, the balloon catheter is inserted gently and carefully through the cervix and up to the uterine fundus. The balloon is then filled with a 5% dextrose solution until the intrauterine pressure is between 90 and 190 mm Hg. Once the pressure stabilizes at 180 mm Hg, the controller is actuated by pressing on the button at the proximal tip of the catheter. A heating element inside the balloon brings the temperature of the fluid to 87°C (± 5°C) for 8 minutes [Amso et al., 1998; Brun et al., 2000; Cooper and Erikson, 2000; HTAC, 2000; Meyer et al., 1998].

Heat transfer through the balloon results in thermocoagulation of the endometrium to a depth of 3 to 5 mm. The balloon catheter is designed to stop automatically if the pressure drops to below 45 mm Hg or rises above 210 mm Hg [Amso et al., 1998; Brun et al., 2000; Cooper and Erikson, 2000; HTAC, 2000; Meyer et al., 1998].

Cavaterm plus System[17]

Originally, the Cavaterm included an 8-mm-diameter catheter, and treatment took 15 minutes. Improvements have since been made to the device, now called the Cavaterm plus, and the catheter has been replaced with another with a smaller diameter (6 mm). As well, the treatment time is shorter. An adjustable silicone balloon is attached to the distal end of the catheter. The balloon contains an internal fluid mixing element that circulates lukewarm fluid and ensures constant temperatures throughout the treatment [Brun et al., 2000; Cooper and Erikson, 2000; Hawe et al., 1999]. The cervix has to be dilated in order to insert the catheter up to the uterine fundus. The balloon is then filled with a 1.5% glycine solution until an intrauterine pressure of 200 to 220 mm Hg is obtained. Once the pressure stabilizes at 200 mm Hg, the controller is actuated. A heating element inside the balloon raises the temperature of the fluid to 78°C (± 5°C) for 10 minutes [Brun et al., 2000; Hawe et al., 1999; Parkin, 2000a].

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[17] When this report was being drafted, the efficacy and safety of this system had not been established in randomized, controlled trials.

MenoTreat System[18,19]

The MenoTreat includes a 7-mm-diameter catheter with an inflatable, silicone balloon at its distal tip. The cervix has to be dilated in order to insert the catheter up to the uterine fundus. The balloon is then filled with normal saline until an intrauterine pressure of 200 ± 10 mm Hg is achieved. A heating element inside the controller brings the temperature of the fluid to 85 ± 3°C for 11 minutes [Ulmsten et al., 2001].

B.6 Hydrothermal endometrial ablation

The following two systems have been designed for hydrothermal ablation: the Hydro ThermAblator and EnAbl. Both consist of a single-use access device and an operational unit.

Hydro ThermAblator Endometrial Ablation System

The software-driven operational unit is attached to a single-use insulated sheath with an outer diameter of 7.8 mm through which a standard 3-mm hysteroscope is inserted [Corson, 2001; FDA, 2001d; Römer and Müller, 1999; Weisberg et al., 2000]. The cervix has to be dilated to 8 mm in order to insert the insulated sheath. The sheath is advanced into the uterine cavity up to internal cervical os with direct hysteroscopic visualization and remains there throughout the ablation. The uterine cavity is then irrigated with room-temperature normal saline, and a diagnostic hysteroscopy is performed to rule out any intrauterine pathology not previously diagnosed. The instruments inserted into the cervix must form a hermetic seal so that none of the solution backflows out of the uterine cavity [das Dores et al., 1999; Fehr et al., 1998; Römer and Müller, 1999; Weisberg et al., 2000].

The normal saline is contained in a 3-L bag suspended from an IV pole. Continuous circulation of the saline is ensured by gravity and a suction pump. The intrauterine pressure depends on the height of the graduated reservoir and the bag. The reservoir should be 115 cm higher than the patient's uterus so that the solution enters the uterine cavity at a pressure of 50 to 55 mm Hg [Corson, 2001; Richart et al., 1999; Weisberg et al., 2000].

The normal saline circulates at a rate of 300 mL/minute so that it remains at the therapeutic temperature when it travels through the tubing and into the uterine cavity. It takes the device approximately three minutes to bring the saline to the desired temperature [Corson, 2001; FDA, 2001d; Fehr et al., 1998; Goldrath et al., 1997; Weisberg et al., 2000]. Timing of the treatment starts as soon as the temperature of the saline reaches 80°C. However, its temperature continues to increase for about one minute until it reaches 90°C. The treatment per se takes about 10 minutes [Corson, 2001; das Dores et al., 1999; FDA, 2001d; Fehr et al., 1998; Richart et al., 1999;

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[18] When this report was being drafted, the efficacy and safety of this system had not been established in randomized, controlled trials.

[19] As at July 31, 2002, this system had not been approved by the HPFB.

Römer and Müller, 1999; Weisberg et al., 2000]. Once the treatment is successfully completed, the operator rinses the uterine cavity with room-temperature normal saline in order to quickly reduce the temperature of the fluid in the uterus and sheath. After about one minute of rinsing, the operator removes the sheath from the uterus. The procedure is then finished [Corson, 2001; FDA, 2001d; Fehr et al., 1998].

Endometrial necrosis is achieved to a depth of 3 to 4 mm in most of the uterine cavity and to 2 to 3 mm in the cornual regions [Richart et al., 1999]. The software-driven operational unit regulates the temperature of the saline, the treatment time, the irrigation flow rate and the drainage rate. It also detects leaks, automatically alerting the operator and interrupting the treatment if more than 10 mL of solution escapes [Corson, 2001; FDA, 2001d; Goldrath et al., 1997 Römer and Müller, 1999; Weisberg et al., 2000].

EnAbl System[20,21]

The EnAbl includes a 6.7-mm-diameter access device that is inserted into the uterine cavity through the cervix. A 5-mm-diameter catheter is then inserted into the uterine cavity through the device and guided in such a way as to permit the deployment of the thermocouple cage at the uterine fundus. The uterus, catheter and tubing are filled with 5 to 15 mL of normal saline. The amount of saline injected depends on the size of the uterus. A decrease in fluid pressure indicates a perforation. The catheter is connected to a 3-mL syringe placed in a Micro-Jet mixer (InnerDyne Medical), which aspirates and reinstills the fluid throughout the treatment. Afterwards, the device heats the fluid, which circulates continuously at a preset temperature of 70 to 85°C. A controller monitors the intrauterine temperature and pressure. The treatment takes about 15 minutes [Baggish et al., 1995; Bustos-Lopez et al., 1998].

B.7 Endometrial cryoablation

The two most important considerations when designing cryosurgical devices are the cryoprobe surface temperature and the cooling speed. The surface temperature of the cryoprobe determines the size of the iceball and the isothermal gradients inside the iceball. Most cells are destroyed at temperatures of −20°C. It is therefore important to achieve a necrotizing temperature at the desired depth. Rapid cooling enhances the technique's destructive capability by causing ice crystals to form in the cells. In general, cooling of at least 15°C per minute causes necrosis. Repeated exposure of tissue to cold stimulates growth of the iceball and necrotizing area and speeds up the cooling process and therefore the necrotizing process [Dobak et al., 2000a].

The Her Option™ and Soprano™ cryotherapy systems have been specifically designed for endometrial ablation in the treatment of dysfunctional uterine bleeding.

Her Option Uterine Cryoblation Therapy System

The operation of the Her Option (previously First Option) System is based on the Joule-Thomson effect. A compressor continuously circulates a mixture of pressurized gases during the operation. The mixture, which consists of common gaseous refrigerants, is nonflammable, noncorrosive and nontoxic. The compressor's operating pressure range is from

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[20] When this report was being drafted, the efficacy and safety of this system had not been established in randomized, controlled trials.

[21] As at July 31, 2002, this system had not been approved by the HPFB.

2,414 to 2,758 kPa. A feedback loop regulates the compressor's stroke length in order to limit the operating pressure to 2,758 kPa or less [FDA, 2001a]. A cryoprobe is connected to the compressor by flexible tubing and is controlled by a single-use, sterile unit (5.5 mm in diameter) whose metal tip fits over the freezing tip of the cryoprobe. The control unit contains a heater wire and a thermocouple. The cryoprobe tip is heated at the end of the treatment in order to remove the cryoprobe from the iceball. Prior to use, the inside of the tip of the control unit is coated with a heat-conducting silicone lubricant [Dobak and Willems, 2000; Dobak et al., 2000a; Dobak et al., 2000b; FDA, 2001a].

The cervix has to be dilated to 6 mm in order to insert the cryoprobe up to the uterine fundus. The gaseous mixture diffuses through a small orifice and cools as its pressure changes. An iceball forms when the temperature of the cryoprobe tip is between −100 and −120°C [FDA, 2001b]. Since growth of the iceball is limited, the tip of the cryoprobe has to be pressed against the uterine fundus close to a cornu to ensure complete destruction of the endometrium, including that in the cornual regions [Dobak and Willems, 2000; Dobak et al., 2000a; Dobak et al., 2000b]. Hysterosonography is performed to check that the cryoprobe is properly positioned in the uterus and to monitor the growth of the iceball during the treatment. As the iceball increases in size, its surface gets closer to the tissues, which are destroyed upon contact with the iceball, whose temperature is −20°C or lower [FDA, 2001b]. The Her Option System permits a destructive temperature (≤ −20°C) at a distance of more than 1 cm from the surface of the cryoprobe and a cooling speed greater than 15°C per minute at a distance of 6 to 9 mm [Dobak et al., 2000a].

Necrosis can be achieved to a depth of 6 to 12 mm [Dobak and Willems, 2000; Dobak et al., 2000a; Dobak et al., 2000b]. The device monitors the operating pressure, the circulation of the gaseous mixture and the surface temperature of the cryoprobe. The first treatment cycle takes four minutes. Depending on the characteristics of the uterus, one to three additional treatment cycles of six minutes' duration may be necessary in order to treat the entire target area [Dobak and Willems, 2000; Dobak et al., 2000b; Sanders, 2000].

Soprano Cryotherapy System[22,23]

Dilatation of the cervix to a diameter of 6 mm is followed by the injection of 10 to 15 mL of lubricant into the uterine cavity. The 5-mm cryoprobe is advanced to the uterine fundus. The treatment takes five minutes. If the uterus is more than 9 cm in length, the treatment must be repeated for three minutes in order to adequately treat the uterine isthmus [Cooper and Erickson, 2000].

B.8 Impedance-controlled endometrial ablation

NovaSure Impedance Controlled Endometrial Ablation System

The NovaSure consists of a single-use device, a radiofrequency controller, a CO_2 canister, a foot switch and a power cord. The single-use device comprises a metal mesh triangular electrode mounted on a frame that is deployed in the uterus. The mesh is

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[22] When this report was being drafted, the efficacy and safety of this system had not been established in randomized, controlled trials.

[23] As at July 31, 2002, this system had not been approved by the HPFB.

made of a stretchable, porous fabric consisting of silver and gold plated on nylon and spandex. The single-use catheter housing the mesh is 7 mm in diameter. The cervix has to be dilated to 8 mm in order to insert the catheter up to the uterine fundus [FDA, 2000f].

The triangular electrode is deployed after it is inserted into the uterine cavity. Suction created by the controller serves to maintain good contact between the uterine mucosa and the electrode before ablation starts and to remove liquids, steam and other gases generated during the treatment, in order to facilitate extensive electrodesiccation [Cooper and Erickson, 2000; FDA, 2001f]. The radiofrequency generator delivers to the electrode constant power of up to 180 W at a frequency of 500 kilohertz (kHz). The controller automatically calculates the power requirement based on the dimensions of the uterus (length and width) [Cooper and Erickson, 2000; FDA, 2001f]. Radiofrequency energy dehydrates and coagulates the endometrium and the underlying superficial myometrium. As the tissue destruction progresses, the electrical impedance of the tissues increases [FDA, 2001f]. The procedure ends automatically when the preset cut-off impedance of 50 ohms is reached at the electrode-tissue interface, indicating that tissue destruction has been achieved to a sufficient depth, or when the total treatment time reaches 120 seconds, whichever comes first [Cooper and Erickson, 2000; FDA, 2001f].

The controller includes a uterine cavity integrity assessment system, which is designed to reduce the risk of complications, such as perforation. After the single-use device is positioned in the uterus, the latter is filled with CO_2, which is insufflated through the device. The uterus is considered intact if the CO_2 pressure in the uterine cavity is maintained for four seconds. In this case, the operator can proceed with the ablation per se [FDA, 2000f].

The minimum length of the electrode array is 4 cm. It follows that treating a uterine cavity less than 4 cm in length would cause thermal injury to the endocervical canal [FDA, 2000f]. The procedure does not require pretreatment endometrial thinning and can be performed at any time during the menstrual cycle, even during menstruation. The preset depth of ablation results in deeper tissue destruction in the uterine body (4.0 to 4.5 mm) and shallower destruction in the cornual regions and near the cervix (2.2 to 2.9 mm) [Cooper and Erickson, 2000]. The treatment takes 40 to 120 seconds (average of about 90 seconds), depending on the thickness of the endometrial tissue [Cooper and Erickson, 2000; FDA, 2001f].

B.9 Endometrial laser intrauterine thermotherapy (ELITT)

GyneLase System[24]

Endometrial laser intrauterine thermotherapy (ELITT) is based on the use of a GyneLase laser diode. The diode contains three fibers, through which laser radiation is diffused to the periphery. The power delivered by the surface unit is much lower than that delivered by the Nd:YAG. In fact, the device provides 5 to 7 W of power per fiber for 420 seconds of exposure. The laser beam is emitted at a wavelength of 830 nm in continuous-emission mode and at an output power of 20 W. The absorbed laser light is converted into heat, which causes endometrial coagulation [Cooper and Erickson, 2000; Donnez et al., 2000].

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[24] When this report was being drafted, the efficacy and safety of this system had not been established in randomized, controlled trials.

The cervix has to be dilated to 7 mm in order to insert the handset (6 mm in diameter) up to the uterine fundus. The laser diode is then activated in order to administer the treatment, which is of a preprogrammed duration of 7 minutes. The diode has an output power of 20 W for the first 90 seconds, 18 W for the next 90 seconds and 16 W for the last 240 seconds [Donnez et al., 2000; Jones et al., 2001].

APPENDIX C

Results of the main studies of the efficacy and safety of endometrial ablation techniques

Table C.1A

Results of uncontrolled clinical studies of laser endometrial ablation: Efficacy results

			Efficacy Results					
Authors and year Country	Study design	Duration of follow-up	Number		Rate of change in menstrual blood loss[b] (%)			Satisfaction rate (%)
			Cohort	Follow-up[a]	Amenorrhea	Hypomenorrhea[c]	Failure[d]	
Lomano et al., 1986 United States	Retrospective	Mean: 6.7 months	75	61 (81.3)	23.0	77.0	0	No data
Gimpelson, 1988 United States	Prospective	3 to 18 months, mean: 8	20	20 (100)	45.0	55.0	0	No data
Goldrath, 1990 United States	Retrospective	No data	324	321 (99.1)	46.4	46.7	6.9	No data
Goldfarb, 1990 United States	Prospective	1 to 2 years	35	35 (100)	60.0	31.4	8.6	No data
Garry et al., 1991 United Kingdom	Prospective	6 months to 3 years	859	479 (55.8)	60.1	31.7	8.2	97.3
Bernhard, 1994 United States	Retrospective	3 to 64 months, mean: 19	78	65 (83.3)	26.6	68.7	4.7	90.8
Erian, 1994 United Kingdom	Prospective	1 to 5 years	2,342	1,866 (79.7)	55.9	37.6	6.5	No data
Garry et al., 1995 United Kingdom	Prospective	6 to 42 months, mean: 15	524	501 (95.6)	28.9	66.2	4.9	83.4
Baggish and Sze, 1996[e], United States	Retrospective	1 to 11 years, mean: 4.5	401	No data	62.1	32.7	5.2	No data
Phillips et al., 1998 United Kingdom	Prospective	26.5 to 76.8 months	873	762 (87.3)	37.6	53.9	8.5	89.3
Everett, 1999 United States	Prospective	12 to 72 months	86	86 (100)	81.4	18.6	0	No data

[a] Percentage (%) of the original cohort who could be followed.

[b] After the first endometrial ablation.

[c] Includes spotting and eumenorrhea.

[d] Menstrual blood loss unchanged or heavier.

[e] Part of a larger cohort including patients treated by rollerball ablation (see Table C.4).

Table C.1B

Results of uncontrolled clinical studies of laser endometrial ablation: Safety results

	Safety results						
Authors and year Country	Reintervention rate (%)		Complication rate[b] (%)				
			Intraoperative complications			Postoperative complications	Total
	Repeat EA[a]	Hysterectomy	Uterine perforation[c]	Fluid overload[d]	Hemorrhage		
Lomano et al., 1986 United States	No data	4.0	1.6	1.6	0	0	3.2
Gimpelson, 1988 United States	5.0	0	0	5.0	0	0	5.0
Goldrath, 1990 United States	3.4	5.9	0.3	1.5	3.9	Hematometra: 3.6 Urinary tract infection: 0.9 Endomyometritis: 0.3 Cervical bleeding: 0.3	10.8
Goldfarb, 1990 United States	2.9	5.7	0	2.9	0	0	2.9
Garry et al., 1991 United Kingdom	1r: 4.8 2r: 0.6	2.8	0.3	0.5	0	Pyrexia: 0.5	1.3
Bernhard, 1994 United States	1.5	6.2	No data	No data	No data	From vaginitis to DVT: 29.2	29.2
Erian, 1994 United Kingdom	4.5	1.8	0.2	1.3	0.3	Infection: 0.6	2.4
Garry et al., 1995 United Kingdom	1r: 14.3 2r: 0.2	6.8	0	5.0	0	Infection: 0.3 Pregnancy: 0.3	5.6
Baggish and Sze, 1996 United States	No data	No data	0	1.0	0.2	Endometritis: 0.2 Pyrexia: 0.5	1.9
Phillips et al., 1998 United Kingdom	1r: 14.2 2r: 0.4	14.6	0	0	0.2	Hematometra: 0.4 Endomyometritis: 0.2	0.8
Everett, 1999 United States	No data	No data	0	1.2	0	0	1.2

[a] EA: Endometrial ablation; r: repeat.

[b] All endometrial ablations combined (initial operations and repeats).

[c] Includes cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

Table C.2A

Results of uncontrolled clinical studies of transcervical resection of the endometrium: Efficacy results

			Efficacy results					
Authors and year **Country**	**Study design**	**Duration of follow-up**	**Number**		**Rate of change in menstrual blood loss[b] (%)**			**Satisfaction rate (%)**
			Cohort	**Follow-up[a]**	**Amenorrhea**	**Hypomenorrhea[c]**	**Failure[d]**	
DeCherney et al., 1987 United States	Prospective	6 months to 5 years	21	18 (85.7)	94.4	5.6	0	No data
Maher and Hill, 1990[e] Australia	Prospective	≥ 6 months	100	98 (98.0)	21.4	75.5	3.1	No data
Magos et al., 1991 United Kingdom	Prospective	3 months to 2.5 years	234	3 months: 203 6 months: 168 9 months: 140 1 year: 113 2 years: 30 2.5 years: 10	27.0 to 42.0[f]	48.0 to 68.0[f]	0 to 10.0[f]	60.0 to 100.0[f]
Pyper and Haeri, 1991 United Kingdom	Prospective	≥ 12 months	80	75 (93.8)	8.0	64.0	28.0	No data
Senden and Brooks, 1991[g] United States	Prospective	3 months to 3 years	96	82 (85.4)	50.0	42.7	7.3	No data
Rankin and Steinberg, 1992[h] United Kingdom	Retrospective	4 months	400	396 (99.0)	No data	No data	No data	84.8

[a] Percentage (%) of the original cohort who could be followed.

[b] After the first endometrial ablation.

[c] Includes spotting and eumenorrhea.

[d] Menstrual blood loss unchanged or heavier.

[e] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy) in 40 patients.

[f] Depending on the duration of follow-up.

[g] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy) in all the patients.

[h] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy) in 196 patients.

Table C.2A (cont'd)

Authors and year Country	Study design	Duration of follow-up	Efficacy results					
			Number		Rate of change in menstrual blood loss[b] (%)			Satisfaction rate (%)
			Cohort	Follow-up[a]	Amenorrhea	Hypomenorrhea[c]	Failure[d]	
Browne, 1996[i] New Zealand	Prospective	1 to 5 years	238	231 (97.1)	48.1	29.0	22.9	No data
O'Connor and Magos, 1996[g], United Kingdom	Prospective	Up to 5 years Mean: 31 months	525	1 year: 524 2 years: 408 3 years: 253 4 years: 146 5 years: 37	26.0 to 40.0[f]	50 to 65.0[f]	0 to 7.0[f]	79.0 to 87.0[f]
Salat-Baroux et al., 1996[g], France	Retrospective	36 months	342	342 (100)	28.4	63.1	8,5	No data
Steffensen and Schuster, 1997[j], Norway	Retrospective	3 to 48 months Mean: 24	250	3 months: 203 12 months: 228 24 months: 155 36 months: 92 48 months: 25	55.0 to 81.0[f]	11.0 to 35.0[f]	No data	91.6
Yin et al., 1998[g] Taiwan	Prospective	6 to 18 months	163	127 (77.9)	18.1	59.9	22.0	63.0

[a] Percentage (%) of the original cohort who could be followed.

[b] After the first endometrial ablation.

[c] Includes spotting and eumenorrhea.

[d] Menstrual blood loss unchanged or heavier.

[f] Depending on the duration of follow-up.

[g] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy) in all the patients.

[i] Part of a larger cohort. The efficacy results for the metal loop alone are presented in this table.

[j] Treatment of the uterine fundus, cornual regions and lateral walls of the uterus with a rollerball electrode in all the patients.

Table C.2B

Results of uncontrolled clinical studies of transcervical resection of the endometrium: Safety results

	Safety results						
	Reintervention rate (%)		Complication rate[b] (%)				
			Intraoperative complications				
Authors and year Country	Repeat EA[a]	Hysterectomy	Uterine perforation[c]	Fluid overload[d]	Hemorrhage	Postoperative complications	Total
DeCherney et al., 1987, United States	4.8	0	0	0	0	0	0
Maher and Hill, 1990 Australia	2.0	0	1.0	0	5.0	Hematometra: 2.0 Infection: 2.0 Pregnancy: 1.0	11.0
Magos et al., 1991 United Kingdom	6.8	4.3	1.6	2.8	0.4	Pregnancy: 0.4	5.2
Pyper and Haeri, 1991 United Kingdom	1r: 17.5 2 r: 1.3	5.0	3.8	3.8	1.3	Secondary hemorrhage: 1.3	10.2
Serden and Brooks, 1991, United States	No data	No data	0	1.1	4.2	Endometritis: 2.1 Persistent pain: 2.1	9.5
Rankin and Steinberg, 1992, United Kingdom	1r: 7.5 2 r: 0.3	6.8	0.5	0	0.9	Unexpected malignant tumor: 0.9 Secondary hemorrhage: 0.2	2.5
Browne, 1996 New Zealand	No data	No data	No data[e]	No data[e]	No data[e]	No data[e]	No data[e]
O'Connor and Magos, 1996, United Kingdom	9.5	8.8	2.7	3.5	0.9	Endometritis: 1.9 Urinary tract infection: 0.5	9.5
Salat-Baroux et al., 1996, France	6.5	9.0	0	0.9	0	Unexpected malignant tumor: 0.6 Febrile syndrome: 0.3	1.8
Steffensen and Schuster, 1997, Norway	3.2	5.2	0.8	0.4	14.3	Infection: 1.3 Unexpected malignant tumor: 0.4	17.2
Yin et al., 1998 Taiwan	5.5	4.7	1.2	0	0.6	Endometritis: 1.8 Pregnancy: 0.6	4.2

[a] EA: Endometrial ablation; r: repeat.

[b] All endometrial ablations combined (initial operations and repeats).

[c] Includes cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

[e] The authors report, in a general manner (for the overall cohort), the intraoperative and postoperative complications.

Table C.3A

Results of randomized, controlled trials of transcervical resection of the endometrium with and without pretreatment with endometrial thinning agents: Efficacy results

Efficacy results								
Authors and year Country	Study design[a]	Duration of follow-up	Number		Rate of change in menstrual blood loss[c] (%)			Satisfaction rate[f] (%)
			Cohort[b]	Follow-up	Amenorrhea	Hypomenorrhea[d]	Failure[e]	
Rai et al., 2000 United Kingdom	Single-centre CG: No thinning[g] EG: Thinning[h] 1) Danazol[i] 2) Medroxyprogesterone[j] 3) Nafarelin[k]	12 months	CG: 25 EG: 1): 25 2): 25 3): 25	CG: 25 EG: 1): 25 2): 25 3): 25	CG: 52.0[l] EG: 1): 68.0[l,m] 2): 28.0[m] 3): 36.0[m]	No data	No data	CG: 100.0 EG: 1): 100.0 2): 100.0 3): 80.0[n]
Kriplani et al., 2002 India	Single-centre CG: No thinning EG: Thinning 1) Danazol[o]	1 to 6 years	CG: 65 EG: 67	CG: 1 year: 62 3 years: 42 6 years: 31 EG: 1 year: 67 3 years: 45 6 years: 30	CG: [l] 1 year: 52 3 years: 52 6 years: 48 EG: [l] 1 year: 49 3 years: 51 6 years: 50	No data	CG: 3.1 EG: 3.0	CG: 98.5 EG: 98.5

[a] CG: Control group; EG: Experimental group.

[b] Number of patients randomized.

[c] After the first endometrial ablation.

[d] Includes spotting and eumenorrhea.

[e] Menstrual blood loss unchanged or heavier.

[f] Patients satisfied or very satisfied.

[g] Preoperative endometrial thinning.

[h] For a period of 8 weeks, starting on the fifth day of the next-to-last menstrual cycle before the operation.

[i] 200 mg every 8 hours.

[j] Medroxyprogesterone acetate, 10 mg every 8 hours, up to one week before the operation in order to induce withdrawal bleeding.

[k] 200 mg every 12 hours.

[l] No significant difference ($P \geq 0.05$).

[m] Significant difference between the groups that received danazol and medroxyprogesterone ($P = 0.02$) or nafarelin ($P = 0.005$).

[n] The comparison between each of the experimental groups and the control group did not reveal any significant differences ($P \geq 0.05$).

[o] 400 to 600 mg per day for 4 to 6 weeks before and 6 weeks after the operation.

Table C.3B

Results of randomized, controlled trials of transcervical resection of the endometrium with and without pretreatment with endometrial thinning agents: Safety results

	Safety results						
	Reintervention rate (%)		Complication rate[b] (%)				
			Intraoperative complications				
Authors and year Country	**Repeat EA[a]**	**Hysterectomy**	**Uterine perforation[c]**	**Fluid overload[d]**	**Hemorrhage**	**Postoperative complications**	**Total**
Rai et al., 2000 United Kingdom	0	CG: 0 EG: 1): 8.0[e] 2): 0 3): 8.0[e]	0	No data	0	No data	No data
Kriplani et al., 2002 India	CG: 1.5 EG: 1.5	CG: 1.5 EG: 1.5	No data	No data	No data	No data	No data

[a] EA: Endometrial ablation.

[b] All endometrial ablations combined (initial operations and repeats).

[c] Includes cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

[e] The authors do not give the results of the statistical analysis.

Table C.4A

Results of uncontrolled clinical studies of rollerball endometrial ablation: Efficacy results

Efficacy results								
Authors and year Country	Study design	Duration of follow-up	Number		Rate of change in menstrual blood loss[b] (%)			Satisfaction rate (%)
			Cohort	Follow-up[a]	Amenorrhea	Hypomenorrhea[c]	Failure[d]	
Daniell et al., 1992 United States	Retrospective	6 to 30 months	64	61 (95.3)	29.5	60.7	9.8	80.3
Fraser et al., 1993 Australia	Prospective	12 months	77	77 (100)	25.0	69.0	6.0	No data
Wortman and Daggett, 1993[e] United States	Prospective	12 months	69	65 (94.2)	55.4	43.1	1.5	No data
Paskowitz, 1995 United States	Prospective	5 years Mean: 2.5	200	No data	40.0	60.0	0	No data
Alford and Hopkins, 1996 United States	Retrospective	12 to 58 months Mean: 32	40	40 (100)	40.0	60.0	0	No data
Baggish and Sze, 1996[f] United States	Retrospective	1 to 11 years Mean: 4.5	167	No data	46.1	40.7	13.2	No data
Chullapram et al., 1996 Australia	Retrospective	12 to 52 months	142	128 (90.1)	25.0	60.9	14.1	84.4
Unger and Meeks, 1996 United States	Retrospective	48 to 60 months	42	41 (97.6)	No data	No data	No data	87.8[g]
Vilos et al., 1996b Canada	Retrospective	12 months	800	728 (91.0)	60.0	35.0	5.0	No data
El Senoun et al., 2000 United Kingdom	Retrospective	18 to 55 months Mean: 32	91	80 (87.9)	43.8	40.0	16.2	78.8
Teirney et al., 2000[h] Australia	Prospective	5 to 6 years Mean: 5.4	39	26 (66.7)	46.2	53.8	0	No data
Dutton et al., 2001 United States	Retrospective	0.25 to 77 months Mean: 31	265	1 year: 195 2 years: 144 3 years: 93 4 years: 56 5 years: 29	91.4 to 96.6[i]	91.4 to 96.6[i]	3.4 to 8.6[i]	No data

[a] Percentage (%) of the original cohort who could be followed.

[b] After the first endometrial ablation.

[c] Includes spotting and eumenorrhea.

[d] Menstrual blood loss unchanged or heavier.

[e] Part of a larger cohort. The results for the rollerball-treated patients with normal hysteroscopic examination results (group 1) are presented in this table.

[f] Part of a larger cohort including patients treated by laser endometrial ablation (see Table C.1).

[g] Satisfaction rate determined two years after the initial operation.

[h] Long-term outcomes in women followed at the Sydney Research Centre until the end of the original study conducted by Fraser et al. [1996].

[i] Treatment outcomes achieved three to five years after the initial operation.

Table C.4B

Results of uncontrolled clinical studies of rollerball endometrial ablation: Safety results

	Safety results						
Authors and year Country	Reintervention rate (%)		Complication rate[b] (%)				
	Repeat EA[a]	Hysterectomy	Intraoperative complications			Postoperative complications	Total
			Uterine perforation[c]	Fluid overload[d]	Hemorrhage		
Daniell et al., 1992 United States	11.5	6.6	1.6	0	0	0	1.6
Fraser et al., 1993 Australia	6.5	3.9	1.2	0	0	Uterine infection: 2.4 Persistent pain: 1.2	4.8
Wortman and Daggett, 1993, United States	1.4	1.4	4.3	0	0	Infection: 1.4	5.7
Paskowitz, 1995 United States	4.0	5.5	0	1.4	1.0	0	2.4
Alford and Hopkins, 1996, United States	2.5	5.0	2.4	0	0	0	2.4
Baggish and Sze, 1996, United States	No data	No data	0	0	No data	No data	No data
Chullapram et al., 1996, Australia	8.5	8.5	Intraoperative complications: 2.8			Postoperative complications: 1.4	4.2
Unger and Meeks, 1996, United States	No data	34.1	0	0	0	0	0
Vilos et al., 1996b Canada	4.4	2.5	1.6	1.0	0.6	Endomyometritis: 0.5 Salpingitis: 0.1 Pregnancy: 0.1	3.9
El Senoun et al., 2000 United Kingdom	0	7.7	2.5	1.3	1.3	0	5.1
Teirney et al., 2000 Australia	0	5.1	No data	No data	No data	No data	No data
Dutton et al., 2001 United States	3.8	17.4	1.9	2.6	0	Endometritis: 1.9 Cervical stenosis: 1.1 Tubo-ovarian abscess: 0.4 Unexpected malignant tumor: 0.4	8.3

[a] EA: Endometrial ablation.

[b] All endometrial ablations combined (initial operations and repeats).

[c] Including cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

Table C.5A

Results of uncontrolled clinical studies of microwave endometrial ablation (MEA): Efficacy results

Efficacy results								
Authors and year Country	Study design	Duration of follow-up	Number		Rate of change in menstrual blood loss[b] (%)			Satisfaction rate (%)
			Cohort	Follow-up[a]	Amenorrhea	Hypomenorrhea[c]	Failure[d]	
Sharp et al., 1995 United Kingdom	Prospective	6 months	23	23 (100)	56.5	26.1	17.4	No data
Hodgson et al., 1999 United Kingdom	Prospective	3 years	43	43 (100)	37.2	48.8	14.0	83.7
Milligan and Etokowo, 1999 United Kingdom	Prospective	12 months	16	16 (100)	18.8	74.9	6.3	87.5
Sharp et al., 2000 United Kingdom	Prospective	6 months to 4 years	236	No data	34.0[e]	No data	No data	82.2

[a] Percentage (%) of the original cohort who could be followed.

[b] After the first endometrial ablation.

[c] Includes spotting and eumenorrhea.

[d] Menstrual blood loss unchanged or heavier.

[e] The authors do not explain how this rate was obtained and calculated.

Table C.5B

Results of uncontrolled clinical studies of microwave endometrial ablation (MEA): Safety results

Safety results							
Authors and year Country	Reintervention rate (%)		Complication rate[b] (%)				
	Repeat EA[a]	Hysterectomy	Intraoperative complications			Postoperative complications	Total
			Uterine perforation[c]	Fluid overload[d]	Hemorrhage		
Sharp et al., 1995 United Kingdom	13.0	0	No data	No data	No data	No data	No data
Hodgson et al., 1999 United Kingdom	7.0	9.3	0	0	0	Intense pain: 4.7	4.7
Milligan and Etokowo, 1999, United Kingdom	0	6.3	0	0	0	Urinary tract infection: 12.5 Purulent vaginal discharge: 6.3 Intense pain: 6.3	25.1
Sharp et al., 2000 United Kingdom	8.1	11.0	0.3	0	0	Endometritis: 0.9	1.2

[a] EA: Endometrial ablation.

[b] All endometrial ablations combined (initial operations and repeats).

[c] Including cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

Table C.6A

Results of uncontrolled clinical studies of thermal balloon endometrial ablation (ThermaChoice): Efficacy results

			Efficacy results					
Authors and year Country	Study design	Duration of follow-up	Number		Rate of change in menstrual blood loss[b] (%)			Satisfaction rate (%)
			Cohort[b]	Follow-up[a]	Amenorrhea	Hypomenorrhea[c]	Failure[d]	
Singer et al., 1994 United Kingdom	Prospective	6 to 34 months	18	18 (100)	44.5	44.4	11.1	No data
Vilos et al., 1996c Canada	Prospective	3 to 18 months	30	30 (100)	3.3	73.4	23.3	No data
Fernandez et al., 1997 France	Prospective	4 to 24 months Mean: 13.9	18	11 (61)	54.5	45.5	0	No data
Vilos et al., 1997b Canada	Prospective	3 to ≥ 12 months	121	121 (100)	22.3	63.6	14.0	No data
Amso et al., 1998 United Kingdom	Prospective	3 to 12 months	296	296 (100)	13.5	75.7	10.8	No data
Buckshee et al., 1998 Inde	Prospective	2 to 19 months	13	13 (100)	15.4	76.9	7.7	84.6[e]
Aletebi et al., 1999 Canada	Prospective	6 to 30 months	46	43 (93.5)	32.6	46.5	20.9	No data
Vilos et al., 2000[f] Canada	Retrospective	12 to 24 months	15	15 (100)	13.3	66.7	20.0	No data
Bongers et al., 2002 Netherlands	Prospective	24 months	141	130 (92.2)	32.0	No data		81.0

[a] Percentage (%) of the original cohort who could be followed.

[b] After the first endometrial ablation.

[c] Includes spotting and eumenorrhea.

[d] Menstrual blood loss unchanged or heavier.

[e] The surgical intervention was considered good or excellent by 8 patients (61.5%) and satisfactory by 3 patients (23.1%).

[f] Part of a larger cohort. The results obtained with the surgical technique of choice (treatment of 8 minutes' duration, intrauterine pressure of 151 to 180 mm Hg) are presented in this table.

Table C.6B

Results of uncontrolled clinical studies of thermal balloon endometrial ablation (ThermaChoice): Safety results

Authors and year Country	Safety results						
	Reintervention rate (%)		Complication rate[b] (%)				
	Repeat EA[a]	Hysterectomy	Intraoperative complications			Postoperative complications	Total
			Uterine perforation[c]	Fluid overload[d]	Hemorrhage		
Singer et al., 1994 United Kingdom	5.6	11.1	0	0	0	Mild abdominal cramping: 5.6	5.6
Vilos et al., 1996c Canada	36.7	6.7	0	0	0	0	0
Fernandez et al., 1997 France	0	0	0	0	0	0	0
Vilos et al., 1997b Canada	14.9	4.1	0	0	0	Endometritis: 2.5 Hematometra: 1.7	4.2
Amso et al., 1998 United Kingdom	4.4	5.1	0	0	0	Endometritis: 2.0 Hematometra: 0.7 Urinary tract infection: 0.3 Intense pain: 0.3	3.3
Buckshee et al., 1998 India	0	15.4	0	0	0	Bradycardia[e]: 7.7 Intense pelvic pain: 7.7	15.4
Aletebi et al., 1999 Canada	9.3	11.6	0	0	0	0	0
Vilos et al., 2000 Canada	No data	No data	0	0	0	Negligible[f]	Negligible[f]
Bongers et al., 2002 Netherlands	No data	12.0	No data	No data	No data	No data	No data

[a] EA: Endometrial ablation.

[b] All endometrial ablations combined (initial operations and repeats).

[c] Includes cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

[e] Occurred during the operation.

[f] The authors state that the postoperative complications were negligible. No data.

Table C.7A

Results of a randomized, controlled trial of thermal balloon endometrial ablation (ThermaChoice) with and without pretreatment with endometrial thinning agents: Efficacy results

Efficacy results								
Authors and year Country	Study design[a]	Duration of follow-up	Number[b]	Rate of change in menstrual blood loss[c] (%)			Days of loss/cycle[f]	Satisfaction rate (%)
				Amenorrhea	Hypomenorrhea[d]	Failure[e]		
Lissak et al., 1999 Israel	Single-centre CG: Thinning[g] EG: No thinning	6 months	CG: 13 EG: 17	CG: 23.1 EG: 23.5 ($P \geq 0.05$)	CG: 76.9 EG: 76.5 ($P \geq 0.05$)	CG: 0 EG: 0 ($P \geq 0.05$)	CG: 1.8 (0.42) EG: 2.1 (0.75) ($P \geq 0.05$)	CG: 84.6 EG: 88.2 ($P \geq 0.05$)

[a] CG: Control group; EG: Experimental group.

[b] No patients lost to follow-up.

[c] After the first endometrial ablation.

[d] Including spotting and eumenorrhea.

[e] Menstrual blood loss unchanged or heavier.

[f] Mean duration of blood loss per menstrual cycle (standard error of the mean).

[g] By intramuscular injection of 3.75 mg of triptorelin pamoate 4 to 6 weeks before the operation.

Table C.7B

Results of a randomized, controlled trial of thermal balloon endometrial ablation (ThermaChoice) with and without pretreatment with endometrial thinning agents: Safety results

Safety results							
Authors and year Country	Reintervention rate (%)		Complication rate[b] (%)				
	Repeat EA[a]	Hysterectomy	Intraoperative complications			Postoperative complications	Total
			Uterine perforation[c]	Fluid overload[d]	Hemorrhage		
Lissak et al., 1999 Israel	CG: 0 EG: 0	CG: 15.3 EG: 5.9[e]	0	0	0	Mild abdominal cramping: CG: 5.0 EG: 5.0[e]	CG: 5.0 EG: 5.0[e]

[a] EA: Endometrial ablation.

[b] All endometrial ablations combined (initial operations and repeats).

[c] Includes cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

[e] The authors do not give the results of the statistical analysis.

Table C.8A
Results of uncontrolled clinical studies of hydrothermal endometrial ablation (HTA): Efficacy results

			Efficacy results					
Authors and year Country	Study design	Duration of follow-up	Number		Rate of change in menstrual blood loss[b] (%)			Satisfaction rate (%)
			Cohort	Follow-up[a]	Amenorrhea	Hypomenorrhea[c]	Failure[d]	
Das Dores et al., 1999 Brazil	Prospective	3 to 18 months	26	3 months: 25 6 months: 22 12 months: 16 18 months: 7	32.0 to 57.1[e]	28.6 to 64.0[e]	4.0 to 14.0[e]	96.0
Römer and Müller, 1999 Germany	Prospective	≥ 12 months	18	18 (100)	50.0	44.4	5.6	94.4
Römer et al., 2000 Germany	Prospective	12 months	64	56 (87.5)	37.0	No data	No data	No data
Weisberg et al., 2000 United States	Prospective	12 months	20	18 (90.0)	50.0	44.4	5.6	No data
Perlitz et al., 2001 Israel	Prospective	9 to 18 months	14	13 (92.9)	84.6	15.4	0	92.3

[a] Percentage (%) of the original cohort who could be followed.

[b] After the first endometrial ablation.

[c] Includes spotting and eumenorrhea.

[d] Menstrual blood loss unchanged or heavier.

[e] Depending on the duration of follow-up.

Table C.8B

Results of uncontrolled clinical studies of hydrothermal endometrial ablation (HTA): Safety results

Authors and year Country	Safety results						
	Reintervention rate (%)		Complication rate[b] (%)				
			Intraoperative complications				
	Repeat EA[a]	Hysterectomy	Uterine perforation[c]	Fluid overload[d]	Hemorrhage	Postoperative complications	Total
Das Dores et al., 1999 Brazil	7.7	3.8	0	0	0	Persistent pain: 25.0	25.0
Römer and Müller, 1999 Germany	0	5.6	0	0	0	0	0
Römer et al., 2000 Germany	No data	No data	0	0	0	Vaginal burning: 3.1	3.1
Weisberg et al., 2000 United States	0	5.0	0	0	0	Abdominal cramping: 15.0	15.0
Perlitz et al., 2001 Israel	7.1	7.1	0	0	0	0	0

[a] EA: Endometrial ablation.

[b] All endometrial ablations combined (initial operations and repeats).

[c] Includes cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

APPENDIX D

Results of the main studies comparing endometrial ablation techniques with hysterectomy

Table D.1A

Results of the meta-analysis of randomized, controlled trials of endometrial ablation techniques and hysterectomy: Operative data and complications

Outcome measures	n[a]	WMD[b]	n	OR[c]
OPERATIVE DATA[d]				
Operating time (minutes)	5	−23.062 [−23.799 to −22.324]		
Length of hospital stay (days)	5	−4.907 [−4.948 to −4.866]		
Time to return to work (weeks)	4	−4.641 [−4.853 to −4.430]		
COMPLICATIONS				
Short-term complications[e,f]				
Sepsis			4	0.16 [0.10 to 0.24]
Hemorrhage			2	0.59 [0.20 to 1.74]
Blood transfusion			3	0.22 [0.08 to 0.57]
Urinary retention			2	0.13 [0.04 to 0.44]
Anemia			1	0.12 [0.03 to 0.43]
Pyrexia			1	0.12 [0.06 to 0.27]
Vaginal vault hematoma			3	0.14 [0.06 to 0.34]
Wound hematoma			1	0.11 [0.04 to 0.32]
Anesthetic			1	0.12 [0.01 to 1.99]
Fluid overload			1	5.57 [1.82 to 17.12]
Perforation			1	6.85 [0.14 to 346.16]
Gastrointestinal obstruction or ileus			1	0.47 [0.05 to 4.58]
Laparotomy			1	0.33 [0.05 to 2.41]
Cautery of hypergranulation			1	0.12 [0.02 to 0.94]
Long-term complications[e,g]				
Sepsis			1	0.19 [0.08 to 0.47]
Hemorrhage			2	7.24 [0.14 to 365.04]
Hematoma			1	0.55 [0.13 to 2.40]
Diarrhea			1	0.13 [0.00 to 6.68]

[a] n: number of trials for which the data are reported.

[b] Weighted mean difference [95% CI].

[c] Odds ratio calculated by the Peto method [95% CI].

[d] A WMD less than 0 indicates a result in favour of endometrial ablation.

[e] An OR less than 1 indicates a result in favour of endometrial ablation.

[f] Prior to discharge from hospital.

[g] After discharge from hospital.

Source: [Lethaby et al., 2000d]

Table D.1B

Results of the meta-analysis of randomized, controlled trials of endometrial ablation techniques and hysterectomy: Treatment outcomes

	Duration of follow-up after the initial intervention							
Outcome measures	n[a]	1 year OR[b]	n	2 years OR	n	3 years OR	n	4 years OR
MENSTRUATION AND SYMPTOMS								
Decrease in menstrual blood loss[c]	3	0.12 [0.06 to 0.25]	1	0.10 [0.00 to 5.41]		No data	1	0.15 [0.01 to 2.38]
Change in quality of life[c]								
Improvement in overall health	1	0.26 [0.11 to 0.63]		No data		No data	1	0.36 [0.13 to 1.01]
Reduction in pain		No data	1	0.54 [0.15 to 1.98]		No data		No data
Relief of symptoms	1	0.43 [0.15 to 1.28]		No data		No data		No data
Need for surgical reintervention[d]	5	7.33 [4.18 to 12.86]	3	7.50 [4.20 to 13.42]	1	4.45 [1.78 to 11.15]	1	9.84 [4.92 to 19.67]
PATIENT SATISFACTION								
With regard to the surgical treatment[c]	3	0.46 [0.24 to 0.88]	3	0.31 [0.16 to 0.59]	1	0.32 [0.08 to 1.37]	1	0.52 [0.21 to 1.26]

[a] n: Number of trials for which data are reported.

[b] Odds ratio calculated by the Peto method [95% CI].

[c] An OR less than 1 indicates a result in favour of hysterectomy.

[d] An OR greater than 1 indicates a result in favour of hysterectomy.

Source: [Lethaby et al., 2000d]

Table D.1C

Results of the meta-analysis of randomized, controlled trials of endometrial ablation techniques and hysterectomy: Quality-of-life measures

Outcome measures	n[a]	WMD[b]
QUALITY-OF-LIFE MEASURES (HIGH VALUE = BENEFIT)[c]		
Golombok Rust Inventory of Marital State		
1 year after the operation	1	0.000 [−1.750 to 1.750]
SF-36		
2 years after the operation		
Limitations due to health problems	2	−1.426 [−10.310 to 7.458]
Limitations due to psychological problems	2	−7.272 [−15.741 to 1.196]
Capacity for social activities	2	−7.182 [−12.387 to −1.977]
Mental health	2	−2.935 [−7.386 to 1.516]
Vitality	2	−5.026 [−10.373 to 0.321]
Pain	2	−8.709 [−15.034 to −2.385]
General health perceptions	2	−6.697 [−12.203 to −1.192]
Physical functional capacity	2	−2.756 [−7.188 to 1.676]
Euroqol		
Change 4 months after the operation	1	−7.000 [−17.286 to 3.286]
2 years after the operation	1	−1.500 [−6.287 to 3.287]
Sabbatsberg Sexual Rating Scale		
2 years after the operation	1	−3.700 [−11.169 to 3.769]
QUALITY-OF-LIFE MEASURES (HIGH VALUE = UNFAVOURABLE)[d]		
HAD		
2 years after the operation	1	1.500 [−1.319 to 4.319]
2 and 4 years after the operation		
Anxiety	2	0.669 [−0.302 to 1.641]
Depression	2	0.002 [−0.092 to 0.096]

[a] n: Number of trials for which data are reported.

[b] Weighted mean difference [95% CI].

[c] A WMD less than 0 indicates a result in favour of hysterectomy.

[d] A WMD greater than 0 indicates a result in favour of hysterectomy.

Source: [Lethaby et al., 2000d]

Table D.2

Results of the case-control study of rollerball endometrial ablation and hysterectomy

Outcome measures	Rollerball ablation	Hysterectomy	P
OPERATIVE DATA[a]	n = 64	n = 46[b]	
Operating time (minutes)	38 (12 to 78)	107 (50 to 165)	< 0.001
Length of hospital stay (days)	0.5 (0.5 to 1)	2.8 (1 to 9)	< 0.001
Length of convalescence (days)[c]	5 (2 to 9)	32 (7 to 84)	< 0.001
COMPLICATIONS (%)	n = 64	n = 46	
Intraoperative complications			≥ 0.05
Uterine perforation[d]	1.6	0	
Fluid overload[e]	3.1	0	
Hemorrhage	0	2.2	
Bladder trauma	0	2.2	
Postoperative complications			≤ 0.05
Endometritis	3.1	0	
Fever	0	13.0	
Urinary tract infection	0	4.3	
Ileus	0	2.2	
Wound hematoma	0	2.2	
Late postoperative complications			No data
Vaginal cellulitis (vault)	0	2.2	
Pelvic abscess	0	2.2	
Hemorrhage from vaginal vault	0	2.2	
Obstruction of the small intestine	0	2.2	
Need for surgical reintervention[f]			
Repeat ablation	3.1		
Hysterectomy	9.4		
Readmissions[g]	12.5	15.2	No data
TREATMENT OUTCOMES (%)			
Duration of follow-up (months)[h]	48.5 (36 to 68)	36	
Change in menstrual blood loss	n = 63	n = 46	No data
Amenorrhea	49.0	100	
Hypomenorrhea or eumenorrhea	38.0	0	
Failure	13.0	0	
Satisfaction with surgical treatment	n = 60	n = 46	
Satisfied	85.0	No data	

[a] Mean value (range).

[b] Including 15 abdominal hysterectomies, 15 vaginal hysterectomies and 16 laparoscopically assisted vaginal hysterectomies.

[c] Return to work or daily activities.

[d] Includes cervical laceration.

[e] Fluid absorption ≥ 1.5 L.

[f] During the three years following the initial operation.

[g] Additional gynecological and surgical admissions.

[h] After the initial operation; mean value (range).

Source: [Hidlebaugh and Orr, 1998]

Table D.3A

Results of the case-control study of rollerball endometrial ablation and abdominal hysterectomy: Operative data and complications

Outcome measures	Rollerball ablation	Abdominal hysterectomy	OR[a]	*P*
OPERATIVE DATA	n = 80	n = 40		
Length of hospital stay (days)[b]	1 (1 to 5)[c]	6 (4 to 11)	No data	
Length of convalescence (%)[d]			No data	
2 weeks	97.5	7.5		
4 weeks	1.25	7.5		
6 weeks	1.25	12.5		
8 weeks	0	55.0		
> 8 weeks	0	17.5		
COMPLICATIONS (%)	n = 80	n = 40		
Intraoperative complications			No data	
Uterine perforation[e]	2.5	0		
Fluid overload[f]	1.3	0		
Hemorrhage	1.3	0		
Postoperative complications			No data	
Wound infection	0	5.0		
Wound hematoma	0	2.5		
Urinary tract infection	0	5.0		
Need for further treatment	12.5[g]	15.0[h]	No data	
Medical treatment	5.0			
Hysterectomy	8.8			

[a] Odds ratio [95% CI].

[b] Median value (range).

[c] Hospitalization of just one patient for 5 days after a laparotomy and uterine perforation repair.

[d] Resumption of daily activities.

[e] Includes cervical laceration.

[f] Fluid absorption ≥ 1.5 L.

[g] Percentage of women who required medical treatment or a hysterectomy.

[h] Percentage of women who required additional surgical or diagnostic intervention.

Source: [Mousa et al., 2001]

Table D.3B

Results of the case-control study of rollerball endometrial ablation and abdominal hysterectomy: Treatment outcomes

Outcome measures	Rollerball ablation	Abdominal hysterectomy	OR[a]	*P*
MENSTRUATION AND SYMPTOMS (%)[b]				
Change in menstrual blood loss	n = 80	n = 40		
Amenorrhea	43.8	100	No data	
Decrease	40.0	0	No data	
No change	7.5	0	No data	
Dysmenorrhea	n = 60	n = 30		
No pain	55.0	83.3	0.2 [0.08 to 0.73]	0.008
Decrease	18.3	16.7	1.1 [0.35 to 3.59]	0.9
Same	23.3	0	10.2 [1.15 to 89.79]	0.01
Worse	3.4	0	1.1 [0.09 to 14.38]	0.9
Premenstrual syndrome	n = 59	n = 33		
Decrease	64.4	87.9	0.3 [0.08 to 0.81]	0.02
Same	20.3	9.1	2.6 [0.67 to 9.80]	0.2
Worse	15.3	3.0	5.8 [0.7 to 47.66]	0.07
SATISFACTION AND LIFESTYLE (%)[b]				
Patient satisfaction	n = 80	n = 40		
Satisfied	78.8	100	0.1 [0.01 to 0.72]	0.005
Dissatisfied	8.7	0	4.3 [0.46 to 39.57]	0.2
Not sure	12.5	0	6.3 [0.71 to 56.83]	0.06
Would recommend the same operation to a friend with a similar problem	91.3	100	0.3 [0.03 to 2.18]	0.2

[a] Odds ratio [95% CI].

[b] Mean follow-up of 32 months after the initial operation (range: 18 to 55 months).

Source: [Mousa et al., 2001]

Table D.3B (Cont'd)

Results of the case-control study of rollerball endometrial ablation and hysterectomy: Treatment outcomes

Outcome measures	Rollerball ablation	Abdominal hysterectomy	OR[a]	*P*
SATISFACTION AND LIFESTYLE (%)[b] (cont'd)				
Sexual functioning	**n = 52**	**n = 38**		
Improvement	96.2	84.2	4.7 [0.89 to 24.67]	0.05
Same	3.8	7.9	0.5 [0.07 to 2.94]	0.4
Worse	0	7.9	0.2 [0.02 to 2.21]	0.2
Ability to perform housework	**n = 65**	**n = 32**		
Improvement	84.6	100	0.2 [0.02 to 1.40]	0.06
Same	15.4	0	6.5 [0.72 to 58.38]	0.06
Decrease	0	0	0	0
Ability to work[c]	**n = 72**	**n = 29**		
Improvement	90.3	100	0.3 [0.03 to 2.70]	0.2
Same	5.5	0	1.9 [0.18 to 11.43]	0.6
Decrease	4.2	0	1.4 [0.13 to 15.37]	0.7

[a] Odds ratio [95% CI].

[b] Mean follow-up of 32 months after the initial operation (range: 18 to 55 months).

[c] If applicable.

Source: [Mousa et al., 2001]

APPENDIX E

Characteristics of controlled studies of endometrial ablation techniques

Table E

Characteristics of controlled studies of endometrial ablation techniques

Study	Design	Participants	Treatments (n)[a]	Outcome measures
Phillips, 1994 United States	Case-control study Single-centre Follow-up of 6 months No statistical analysis	166 women treated between March 1986 and October 1992 13 lost to follow-up (7.8%) Indications: Menorrhagia (complete clinical evaluation), lack of response to medical treatment, high risk associated with hysterectomy, persistent postmenopausal bleeding interfering with hormone substitution therapy Contraindications: Cancer or precancerous lesion of the endometrium, desire to preserve fertility, uterine cavity >12 cm in length	CG: Transcervical resection[b] (97) or rollerball ablation (11) EG: Laser ablation (58) Endometrial thinning with danazol or leuprolide acetate (1986 to 1988) or leuprolide acetate, 1 to 3 doses/month up to 3 to 4 weeks before and 1 dose 1 to 7 days after the operation (1988 to 1992)	Primary: Operating time and length of hospital stay, complications, volume of irrigation fluid absorption, relief of menstruation flow, need for surgical reintervention. Satisfactory results defined as having become amenorrheic, hypomenorrheic or eumenorrheic.
Bhattacharya et al., 1997 United Kingdom	Randomized, controlled trial (method described and acceptable) Single-centre Follow-up of 12 months Intention-to-treat analysis	372 subjects 51 dropouts (13.7%) Inclusion criteria: Subjective complaints of intolerable menstrual loss, age ≤ 50 years, weight < 100 kg, clinical diagnosis of dysfunctional uterine bleeding (uterine size < 10 weeks' gestation and histologically normal endometrium)	CG: Transcervical resection[c] (184) EG: Laser ablation (188) Endometrial thinning with the administration of 3.6 mg of goserelin acetate 5 weeks before the operation	Primary: Intraoperative complications, postoperative recovery, relief of menstrual and other symptoms, need for further surgical treatment, patient satisfaction and resource utilization. Evaluation, 6 and 12 months after the initial operation, of menstrual blood loss and other symptoms by means of a clinical questionnaire, and of the psychological effects on the HAD scale. Degree of uterine bleeding and of pain assessed on a 5-point scale each day of the period, and scores added to give a total score. Also, satisfaction measured, and costs incurred by the patient (lost wages, child care and travel expenses, as well as savings on sanitary napkins) determined. Reintervention data taken from the operating suite database and case note review.

[a] CG: Control group; EG: Experimental group.

[b] Entire endometrial surface treated with a metal loop, then with a rollerball electrode.

[c] Uterine walls treated with a metal loop, and the uterine fundus and the cornual regions with a rollerball electrode.

Table E (Cont'd)

Study	Design	Participants	Treatments (n)[a]	Outcome measures
Overton et al., 1997 United Kingdom	Prospective survey[d] Multicentre[e] Statistical analysis on a patient basis and of those cases where the fields had been completed satisfactorily	10,686 women registered by 690 physicians between April 1993 and October 1994	Laser ablation (1,793) Transcervical resection (3,776) Rollerball ablation (650) Combined diathermy[c] (4,291) Radiofrequency ablation (140) Cryoablation (36) Endometrial thinning with pharmacologic agents in more than 87% of the subjects	Primary: Intraoperative, postoperative and delayed complications by method of surgery and operator experience. Questionnaire for obtaining as much information as possible on previous experience and training sent to all the physicians (consultants and residents) performing endometrial ablations. Clinical and surgical observations recorded for each woman treated by endometrial ablation on a data form, which was returned to the investigators. Clinical and surgical data entered into a computer and cases cross-checked. List of missing data forms sent to the physicians' secretarial contact in order to obtain a higher rate of return.

[a] CG: Control group; EG: Experimental group.

[c] Uterine walls treated with a metal loop, and the uterine fundus and the cornual regions with a rollerball electrode.

[d] With additional retrospective reporting by operating room staff.

[e] 300 National Health Service and independent hospitals in the United Kingdom (excluding Scotland).

Table E (Cont'd)

Study	Design	Participants	Treatments (n)[a]	Outcome measures
Meyer et al., 1998 United States Grainger et al., 2000 United States Loffer, 2001 United States	Randomized, controlled trial (method described and acceptable) Multicentre Follow-up of 12, 24 and 36 months Per-protocol analysis	275 subjects randomized 36 dropouts (13.1%) after 12 months 48 dropouts (17.5%) after 24 months 61 dropouts (22.2%) after 36 months Inclusion criteria: Premenopausal, age ≥ 30 years, normal vaginal smear and endometrial biopsy (within previous 6 months), documented history of dysfunctional uterine bleeding (of at least 3 months' duration), no histopathologic abnormalities of the endometrium (confirmed by transvaginal ultrasound, hysteroscopy or hysterosalpingography), uterine cavity 4 to 10 cm in length, childbearing complete, and willing to continue using the present method of contraception for 3 years after the endometrial ablation. Exclusion criteria: Previous endometrial ablation, a history of submucous uterine fibroids, suspected genital infection, or cancer.	CG: Rollerball ablation (138) EG: Thermal balloon ablation *(ThermaChoice)* (137) No pretreatment with endometrial thinning agents 3-minute curettage before both ablation techniques	Primary: Reduction in menstrual flow (Higham diary score[f] ≤ 75). Secondary: Patient satisfaction, impact of uterine bleeding on quality of life and ability to work outside the home. Menorrhagia was documented prospectively using the pictorial chart method. Blood loss assessed daily with chart (degree to which napkins and tampons were soiled with blood, then conversion to a Higham diary score (150 = menorrhagia = inclusion criteria). Preoperative assessment of the impact of uterine bleeding on quality of life using a 10-point scale (10 = greatest impact). Assessment of the impact of menorrhagia on the ability to work outside the home. Day procedure in all cases. Telephone call within 24 hours following the procedure. Physical examination 1week and 3, 6 and 12 months after the initial ablation. Impact of uterine bleeding reassessed at each visit. Menstrual flow measured (diary scores) with pictorial chart method for 12 months after the operation. After the 12th month and until the end of the 36-month follow-up, evaluation of menstrual blood loss during each interview based on data provided by the patient. Patients questioned and sometimes examined 2 and 3 years after the initial ablation.

[a] CG: Control group; EG: Experimental group.

[f] [Higham et al., 1990].

Table E (Cont'd)

Study	Design	Participants	Treatments (n)[a]	Outcome measures
Cooper et al., 1999a United Kingdom Bain et al., 2002 United Kingdom	Randomized, controlled trial (method described and acceptable) Single-centre Follow-up of 12 and 24 months Intention-to-treat analysis	263 subjects randomized 23 dropouts (8.7%) after 12 months 14 dropouts (5.3%) after 24 months Inclusion criteria: Premenopausal, childbearing completed, subjective complaints of intolerable menstrual loss, dysfunctional uterine bleeding, uterine size ≤ 10 weeks' gestation, no histopathologic abnormalities of the endometrium	CG: Transcervical resection[c] (134) EG: Microwave ablation (MEA) (129) Endometrial thinning with 3.6 mg of goserelin acetate 5 weeks before the operation	Primary: Patient satisfaction and acceptability of the surgical treatment. Secondary: Effects on menstruation and quality of life (SF-36), operative data, morbidity. Clinical questionnaire and evaluation of quality of life (SF-36) during recruitment. Degree of uterine bleeding and pain assessed on a 5-point scale for each day of the period, and scores added to arrive at a total score. Questions concerning bladder and bowel symptoms in order to determine any therapeutic effect of microwaves on these organs. Questionnaire concerning the operation (length, complications, need for postoperative analgesia and length of hospital stay). Checkup visit at the hospital 4 months after the initial intervention. Follow-up by postal questionnaires 12 and 24 months after the initial operation. Questionnaires administered at study entry, including additional questionnaires on patient satisfaction and treatment acceptability, administered during subsequent visits as well.
Gervaise et al., 1999 France	Case-control study Single-centre Patient follow-up: CG: 3 to 36 months (median: 18.3 months) EG: 3 to 44 months (median: 19.2 months)	147 women treated between November 1994 and April 1998 None lost to follow-up Inclusion criteria: Age ≥ 40 years, failure of or refusal to accept progestin treatment, or intolerable adverse effects (premenopausal); desire to continue hormone replacement therapy (postmenopausal women) Exclusion criteria: Submucous uterine fibroids, polyps, precancerous lesions of the endometrium, desire to maintain fertility, uterine cavity > 12 cm in length	CG: Transcervical resection[c] (74) EG: Thermal balloon ablation *(ThermaChoice)* (73) No preoperative endometrial thinning	Primary: Effects on menstruation. Secondary: Effects on dysmenorrhea (in the women who were dysmenorrheic before the initial operation). Telephone call to the patients who underwent balloon ablation 3, 6 and 12 months after the initial procedure, then once a year. Call to check on control group just once. During the telephone interview, the patients were asked about menstrual flow patterns, the number of sanitary napkins used per cycle, and the degree of dysmenorrhea. Assessment of the need for further treatment.

[a] CG: Control group; EG: Experimental group.

[c] Uterine walls treated with a metal loop, and the uterine fundus and the cornual regions with a rollerball electrode.

Table E (Cont'd)

Study	Design	Participants	Treatments (n)[a]	Outcome measures
Bongers et al., 2000 Netherlands	Nonrandomized, controlled, prospective study Single-centre Follow-up of 24 months Intention-to-treat analysis	152 women treated between 1992 and 1997 None lost to follow-up Indications: Menorrhagia, no response to medical treatment Contraindications: Septate uterus, intrauterine adhesions, submucous uterine fibroids, uterine cavity > 12 cm in length	CG: Transcervical resection[c] (75) EG: Thermal balloon ablation *(ThermaChoice)* (77) Endometrial thinning with the administration of GnRH analogs 8 to 12 weeks before the operation (CG) or endometrial curettage (EG)	Primary: Need for surgical reintervention, effects on menstruation and symptoms, patient satisfaction. Data gathered on reintervention. Follow-up visits of 20 minutes' duration 3, 6, 12 and 24 months after the initial intervention, and data gathered on the length of periods, dysmenorrhea and patient satisfaction. Satisfaction evaluated on a 4-point scale (perfectly satisfactory, satisfactory, no therapeutic effect, worsening).
Corson, 2001 United States	Randomized, controlled trial (2:1; method described and acceptable) Multicentre Follow-up of 12 months Intention-to-treat and per-protocol analyses	276 subjects randomized 26 dropouts (9.4%) after 12 months Inclusion criteria: 30 to 50 years of age, childbearing completed, documented history of dysfunctional uterine bleeding (of at least 3 months' duration), failure of or refusal to accept medical treatment, or intolerable adverse effects, mean diary score ≥ 150 for 3 months (never dropping below 100), uterine cavity ≤ 10.5 cm in length. Exclusion criteria: Previous endometrial ablation or classic cesarean section, acute or chronic pelvic infection, acute genital or urinary tract infection, coagulation disorder, hemostatic disorder or anticoagulant therapy, abnormal vaginal smear, histopathologic abnormalities of the endometrium (confirmed by endometrial biopsy), history of cancer of the genital tract within the previous 5 years, submucous fibroids or polyps, intramural fibroid > 4 cm, hydrosalpinx, absolute desire for amenorrhea.	CG: Rollerball ablation (89) EG: Hydrothermal ablation (HTA) (187) Endometrial thinning with the administration of 7.5 mg of leuprolide acetate on the 21st day (± 2 days) of the menstrual cycle Ablation performed 19 to 27 days after endometrial thinning	Primary: Reduction in menstrual flow (Janssen diary score[g] ≤ 75). Secondary: Total percent decrease in the Janssen diary score, quality of life, and safety (including technical malfunctions). Menorrhagia documented prospectively using the pictorial chart method. Blood loss evaluated daily with chart (degree to which pads and tampons were soiled with blood), then conversion to a Janssen diary score. Pregnancy test performed before pharmacological endometrial thinning and on the day of the operation. Preoperative quality-of-life evaluation with questionnaire (scores from 0 to 43; 0 = no effect). Data then converted to a score on a 100-point scale. All subjects examined 2 weeks after the ablation. Physical examination repeated 3, 6 and 12 months after the initial operation. Evaluation of menstrual blood loss (Janssen diary scores) using the pictorial chart method until the end of the 12-month posttreatment follow-up. Quality-of-life questionnaire repeated during subsequent visits.

[a] CG: Control group; EG: Experimental group.

[c] Uterine walls treated with a metal loop, and the uterine fundus and the cornual regions with a rollerball electrode.

[g] [Janssen et al., 1995].

Table E (Cont'd)

Study	Design	Participants	Treatments (n)[a]	Outcome measures
FDA, 2001b[h] United States	Randomized, controlled trial (2:1; method described and acceptable) Multicentre Follow-up of 12 months Intention-to-treat and per-protocol analyses[i]	279 subjects randomized 24 dropouts (8.6%) at 12 months Inclusion criteria: Premenopausal, between 30 and 50 years of age, in good health, documented history of dysfunctional uterine bleeding (of at least 3 months' duration), failed medical treatment or curettage, diary score > 150 for at least one menstrual cycle, or refusal of medical treatment or curettage and diary score > 150 for at least 3 consecutive months, uterine cavity ≤ 10 cm in length, uterine size ≤ 300 cm^3, does not wish to maintain fertility Exclusion criteria: Previous endometrial ablation or uterine surgery that can cause myometrial weakening, acute pelvic inflammatory disease, clotting defects or bleeding disorders, abnormal pap smear within the previous year, positive histopathological study of the endometrium within the previous 6 months (as documented by endometrial biopsy), history of gynecological cancer within the past 5 years, pedunculated uterine fibroids, intrauterine polyps, septate uterus, intramural fibromyomas > 2 cm, pregnancy	CG: rollerball ablation (86) EG: cryoablation (Her Option) (193) Endometrial thinning with the administration of leuprolide acetate 28 days before the operation	Primary: Reduction in menstrual blood loss (Higham diary score[f] ≤ 75). Secondary: Quality of life and safety (including technical malfunctions). Menorrhagia was documented prospectively using the pictorial chart method. Blood loss evaluated daily with chart (degree to which pads and tampons were soiled with blood), then conversion to a Higham diary score. Quality-of-life questionnaires (SF-36 and Dartmouth COOP) before the operation (scale of 1 to 5; 0 = no effect). Evaluation of menstrual blood loss with pictorial chart method (Higham scores) up to the end of the 12 month posttreatment follow-up period. Quality-of-life questionnaires repeated 6 and 12 months after the initial operation. After conditional FDA approval, these questionnaires were to be completed 24 and 36 months after the initial operation as well.

[a] CG: Control group; EG: Experimental group.

[f] [Higham et al., 1990].

[h] The results of this randomized, controlled trial had not been published as at July 31, 2002.

[i] The *P* values are not given.

Table E (Cont'd)

Study	Design	Participants	Treatments (n)[a]	Outcome measures
FDA, 2001f[h] United States	Randomized, controlled trial (2:1; method described and acceptable) Multicentre Follow-up of 12 months Intention-to-treat and per- protocol analyses[i]	265 subjects randomized 27 dropouts (10.2%) after 12 months Inclusion criteria: Premenopausal, between 30 and 50 years of age, refractory menorrhagia with no definable organic cause, diary score ≥150 for 3 months prior to study entry or for 1 month for women who had failed medical treatment during 3 consecutive months or who had a contraindication to medical treatment, uterine cavity 6.0 to 10.0 cm in length Exclusion criteria: Previous endometrial ablation or uterine surgery that can cause myometrial weakening, pharmacological treatment that can cause thinning of the myometrial muscle, coagulopathies or anticoagulant therapy, symptomatic endometriosis, cervical dysplasia, endometrial hyperplasia (histologically confirmed), suspected or confirmed uterine cancer or confirmed uterine cancer within the previous 5 years (histologically confirmed), active sexually transmitted disease, acute or recurrent pelvic inflammatory disease, bacteremia, septicemia or other active systemic infection, abnormal/obstructed uterine cavity as confirmed by hysteroscopy, transvaginal ultrasound or hysterosalpingography (septate or bicornuate uterus or other congenital malformation, pedunculated, submucous leiomyomas distorting the uterine cavity, polyps > 2 cm that are likely to be the cause of the patient's menorrhagia), desire to preserve fertility, pregnancy, hormonal birth control or unwilling to use nonhormonal contraception after endometrial ablation	CG: Transcervical resection[c] (90) EG: Impedance-controlled ablation *(NovaSure)* (175) No preoperative endometrial thinning (ablation performed at any time during the menstrual cycle)	Primary: Reduction in menstrual blood loss (Higham diary score[f] ≤75). Secondary: Procedure time, satisfaction (quality of life and menstrual impact), amenorrhea rate and safety (including technical malfunctions). Menorrhagia was documented prospectively using the pictorial chart method (up to the end of the 12-month posttreatment follow-up). Blood loss evaluated daily with chart (degree to which pads and tampons were soiled with blood), then conversion to a Higham diary score. Complications and adverse events recorded. Protocol deviations and technical malfunctions were recorded. Quality-of-life questionnaire completed before treatment and at 3, 6 and 12 months after the initial operation. After conditional FDA approval, questionnaire to be completed at 24 and 36 months after the initial operation as well.

[a] CG: Control group; EG: Experimental group.

[c] Uterine walls treated with a metal loop, and the uterine fundus and the cornual regions with a rollerball electrode.

[f] [Higham et al., 1990].

[h] The results of this randomized, controlled trial had not been published as at July 31, 2002.

[i] The *P* values are not given.

Table E (Cont'd)

Study	Design	Participants	Treatments (n)[a]	Outcome measures
Boujida et al., 2002 Denmark	Randomized, controlled trial (method described and acceptable) Single-centre Follow-up of 24 and 60 months Intention-to-treat analysis	120 subjects randomized 11 dropouts (9.2%) after 24 months 7 dropouts (5.8%) after 60 months Inclusion criteria: Age > 35 years, dysfunctional uterine bleeding whose severity would justify a hysterectomy if endometrial ablation was not possible Exclusion criteria: Uterine volume more than twice normal, uterine cavity > 12 cm in length, intense pelvic pain, uncertainty as to desire to become pregnant in the future	CG: Transcervical resection[c] (59) EG: Rollerball ablation (61) Endometrial thinning in 111 subjects with the administration of 5 mg/day of norethisterone from the 8th day of the menstrual cycle until the operation (about 14 days later) No preoperative endometrial thinning in 9 subjects	Primary: Hysterectomy rate after 60 months of follow-up. Secondary: Complications, need for surgical reintervention, improvement in menstruation flow, patient satisfaction and acceptability of the treatment. Evaluation of uterine bleeding converted to a uterine bleeding index (number of days of bleeding in a 3-month period). Complications recorded. Control visit at the hospital and follow-up by means of a questionnaire mailed 24 and 60 months after the initial intervention. Questionnaires from the beginning of the study, including additional questions on the patients' satisfaction and the acceptability of the treatment (Would you recommend the treatment to other women?) repeated during subsequent visits.

[a] CG: Control group; EG: Experimental group.

[c] Uterine walls treated with a metal loop, and the uterine fundus and the cornual regions with a rollerball electrode.

APPENDIX F

Results of nonrandomized, controlled studies of endometrial ablation techniques

Table F.1

Results of the case-control study of laser endometrial ablation, rollerball endometrial ablation and transcervical resection of the endometrium

Outcome measures[a]	Laser ablation	Rollerball ablation	Transcervical resection
OPERATIVE DATA	n = 58	n = 11	n = 97
Operating time (minutes)	36	33	28
Length of hospital stay ≤ 24 hours (%)	91.4	90.9	99.1
Irrigation fluid administered (L)	4.20	3.77	3.96
Irrigation fluid absorbed (L)	0.872	0.767	0.801
COMPLICATIONS (%)	n = 58	n = 11	n = 97
Intraoperative complications			
Uterine perforation[b]	1.7	0	0
Fluid overload[c]	10.3	0	2.0
Hemorrhage	0	0	0
Postoperative complications			
Hematometra	0	0	0
Infection	0	0	0
Cervical stenosis	0	0	0
Reintervention rate			
6 months after the initial operation			
Repeat ablation	3.6	9.1	3.5
Hysterectomy	No data	No data	No data
4 years after the initial operation			
Repeat ablation	No data	No data	No data
Hysterectomy	2.1	11.1	0
TREATMENT OUTCOMES 6 MONTHS AFTER THE INITIAL OPERATION (%)	n = 56	n = 11	n = 86
Change in menstrual blood loss			
Amenorrhea	69.6	63.6	70.9
Hypomenorrhea or eumenorrhea	26.8	27.3	25.6
Satisfactory outcomes[d]			
After one ablation	96.4	90.9	96.5
After one or two ablations	98.2	90.9	98.8
TREATMENT OUTCOMES 4 YEARS AFTER THE INITIAL OPERATION (%)	n = 47	n = 9	n = 26
Satisfactory outcomes	87.2	77.8	84.6

[a] The investigator did not perform a statistical analysis of the data.

[b] Includes cervical laceration.

[c] Fluid absorption ≥ 1.5 L

[d] Defined as becoming amenorrheic, hypomenorrheic or eumenorrheic.

Source: [Phillips, 1994]

Table F.2

Results of the nonrandomized, controlled, prospective study of thermal balloon endometrial ablation (ThermaChoice) and transcervical resection of the endometrium

Outcome measures	ThermaChoice	Transcervical resection[a]	*P*
COMPLICATIONS (%)	n = 77	n = 75	
Intraoperative complications			
Uterine perforation[b]	0	1.3	No data
Fluid overload[c]	0	4.0	No data
Hemorrhage	0	1.3	No data
Aborted procedures	10.4	17.3	Not significant
Need for further surgery			0.11[d]
Repeat ablation	0	5.3	
Hysterectomy	11.7	20.0	
TREATMENT OUTCOMES (%)	n = 77	n = 75	
Change in menstrual blood loss			
Amenorrhea			No data
3 months after the initial operation	17	36	
6 months after the initial operation	15	22	
12 months after the initial operation	16	26	
24 months after the initial operation	13	17	
Patient satisfaction			
Perfectly satisfied			0.3
3 months after the initial operation	66	80	
6 months after the initial operation	63	57	
12 months after the initial operation	63	52	
24 months after the initial operation[e]	60	43	

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[b] Including cervical laceration.

[c] Fluid absorption ≥ 1.5 L.

[d] Log-rank test.

[e] Significant decline in patient satisfaction over time ($P = 0.001$).

Source: [Bongers et al., 2000]

Table F.3

Results of the case-control study of thermal balloon endometrial ablation (ThermaChoice) and transcervical resection of the endometrium

Outcome measures	ThermaChoice	Transcervical resection[a]	*P*
OPERATIVE DATA	n = 73	n = 74	
Operating time (minutes)[b]	20.3	44.8	< 0.05
COMPLICATIONS (%)	n = 73	n = 74	
Intraoperative complications			
Uterine perforation[c]	0	0	
Fluid overload[d]	0	0	
Hemorrhage	0	0	
Postoperative complications			
Endometritis	0	2.7	No data
Pregnancy	1.4	0	No data
Need for further treatment			
Medical treatment (progestins)	5.5	9.5	No data
Repeat ablation	0	1.3	No data
Hysterectomy	9.6	6.8	No data
TREATMENT OUTCOMES IN ALL THE SUBJECTS (%)	n = 73	n = 74	
Duration of follow-up (months)[e]	18.3 (± 2.7) (3 to 44)	19.2 (± 2.3) (3 to 36)	
Change in menstrual blood loss			
Amenorrhea	24.7	37.8	Not significant
Hypomenorrhea	21.9	31.1	Not significant
Eumenorrhea	38.3	13.5	0.0006
Treatment failure[f]	15.1	17.6	Not significant
Dysmenorrhea	No data	No data	
TREATMENT OUTCOMES 24 MONTHS AFTER THE INITIAL OPERATION (%)[g]	n = 44	n = 47	
Change in menstrual blood loss			
Amenorrhea	36.4	38.3	No data
Hypomenorrhea	15.9	27.7	No data
Eumenorrhea	34.1	17.0	0.06
Treatment failure	13.6	17.0	No data
Dysmenorrhea	No data	No data	

[a] Uterine fundus and cornual regions treated with a rollerball electrode (combined diathermy).

[b] From the induction of anesthesia to the end of the surgical procedure.

[c] Includes cervical laceration.

[d] Fluid absorption ≥ 1.5 L.

[e] After the initial operation; median value (± SD) (range).

[f] Persistence of uterine bleeding (menorrhagia or metrorrhagia).

[g] Does not include the women who required surgical reintervention.

Source: [Gervaise et al., 1999]

APPENDIX G

Characteristics and results of economic evaluations of endometrial ablation techniques

Table G

Characteristics and results of economic evaluations of the first-generation endometrial ablation techniques and hysterectomy

Authors and year Country	Design	Participants	Treatments (n)[a]	Types of costs	Results[b]		
					Endometrial ablation	Hysterectomy	P
Gannon et al., 1991 United Kingdom	Efficacy data taken from a randomized, controlled trial Single-centre EG: follow-up of 12 months (9 to 16) after the initial operation[c] Hospital perspective, £ [d]	Menorrhagic women with no pelvic pathology on a waiting list for an abdominal hysterectomy	CG: Abdominal hysterectomy (26) EG: Transcervical resection (25)	Direct costs: Variable costs (mean cost of medical supplies, personnel and operating room maintenance, marginal cost of a bed in the gynecology ward) and fixed costs (capital cost depreciation, hospital personnel and energy)	£ 407	£ 1,270	No data
Sculpher et al., 1993 United Kingdom Sculpher et al., 1996 United Kingdom	Economic evaluation running alongside a randomized, controlled trial [Dwyer et al., 1993] Single-centre Follow-up of randomized subjects: 4 months and 2.2 years after the initial operation Health-care system perspective, in £ , 1991-1992 and 1994[e]	Women under the age of 52 with menorrhagia that was not managed with conservative treatment and who were candidates for a hysterectomy, uterine cavity < 12 cm in length, no symptoms or other conditions for which hysterectomy is the treatment of choice	CG: Abdominal hysterectomy (97 at 4 months; 70 at 2.2 years) EG: Transcervical resection (99 at 4 months; 78 at 2.2 years)	Direct costs: Drugs (including hormone replacement therapy), operating room (including personnel, medical supplies and technical equipment), hospitalization (including intensive care unit) and laboratory tests, anesthesia, professional fees, complications (including blood transfusions), additional operations, and medical consultations during the 4 months and 2.2 years following the initial operation	After 4 months: £ 560.05 (± £ 261.22) After 2.2 years: £ 790 (± £ 493)	After 4 months: £ 1,059.73 (± £ 198.04) After 2.2 years: £ 1,110 (± £ 168)	Signif.[f] 0.0001

[a] CG: Control group; EG: Experimental group.

[b] Per patient, including the costs associated with additional operations and with intraoperative and postoperative complications; mean value (± SD)(range).

[c] Mean duration (range). Duration of follow-up in the control group not indicated.

[d] Year not indicated.

[e] Health-care system resources used for the additional operations. Discounted on the basis of the amount of time since randomization (rate of 6%) [Sculpher et al., 1996].

[f] Signif.: Significant (P value not given). Mean difference between the experimental and control groups = − £ 499.68 [95% CI: − 567 to − 432].

Table G (Cont'd)

Authors and year Country	Design	Participants	Treatments (n)[a]	Types of costs	Results[b]		
					Endometrial ablation	Hysterectomy	*P*
Brooks et al., 1994 United States	Retrospective Follow-up from 6 months before to 12 months after the initial operation Third-party payer perspective, $US[d]	Women covered by one of four plans of a national health insurance company and treated for uterine bleeding by endometrial ablation or hysterectomy between 1990 and the middle of 1992	CG: Abdominal (178) or vaginal (77) hysterectomy EG: Transcervical resection or rollerball ablation (85)	Direct costs: Additional diagnostic examinations, medical consultations, drugs for preoperative thinning and other drugs, operation, hospitalization, professional fees, anesthesia, complications, additional operations	Preoperative[g]: $550 US Perioperative: $2,467 US Postoperative: $722 US	Preoperative: $559 US Perioperative: $5,679 US Postoperative: $174 US	No data
Brumsted et al., 1996 United States	Retrospective Single-centre EG: follow-up of 45.4 months (19.1 to 78.7) after the initial operation[c] Societal perspective, 1993, $US	Women treated for uterine bleeding by endometrial ablation or hysterectomy between June 1, 1987 and June 1, 1992	CG: Abdominal (192) or vaginal (37) hysterectomy EG: Laser or rollerball ablation or transcervical resection (60)	Direct costs: Drugs for preoperative thinning and other drugs, operating room, recovery room and hospitalization, professional fees, anesthesia, laboratory tests, medical supplies, complications, additional operations Indirect costs: Lost productivity[h]	Direct costs: $5,159 US Indirect costs: At home: $129 US At work: $315 US	Direct costs: Abdominal approach: $8,833 US Vaginal approach: $8,132 US Indirect costs: Abdominal approach: At home: $1,806 US At work: $4,410 US Vaginal approach: At home: $1,204 US At work: $2,940 US	≤ 0.05 ≤ 0.05 No data No data

[a] CG: Control group; EG: Experimental group.

[b] Per patient, including the costs associated with additional operations and with intraoperative and postoperative complications; mean value (± SD)(range)

[c] Mean duration (range). Duration of follow-up in the control group not indicated.

[d] Year not indicated.

[g] Direct costs during the follow-up periods; preoperative, 180 to 5 days before the initial operation; perioperative, 5 days before to 5 days after the operation; postoperative, 6 to 365 days after the operation.

[h] During convalescence; the indirect costs vary with the length of the convalescence, the workers' annual salary, the annual value of housework for women at home and the percentage of women in a given age group who are at home or in the workforce.

Table G (Cont'd)

Authors and year Country	Design	Participants	Treatments (n)[a]	Types of costs	Results[b]		
					Endometrial ablation	Hysterectomy	P
Cameron et al., 1996 United Kingdom Grant et al., 1999 United Kingdom	Economic analysis alongside a randomized, controlled trial [Pinion et al., 1994] Single-centre Follow-up of 12 months and 4 years after the initial operation Health-care system and patient perspectives, 1994 £[i]	Women aged 50 or less and weighing < 100 kg, clinical diagnosis of menometrorrhagia (uterine size < 10 weeks' gestation and histologically normal endometrium), candidates for a hysterectomy	CG: Abdominal (87) or vaginal (12) hysterectomy EG: Laser ablation (53) or transcervical resection (52)	Direct costs: Preoperative endometrial thinning, operating room, gynecology ward, hospitalization and laboratory tests, professional fees, anesthesia, technical equipment, complications, additional operations and consultations in general medicine or gynecology during the 12 months and 4 years following the initial operation, patients' expenses (lost wages, child care and travel, savings on sanitary napkins)	After 12 months: Health-care system: Laser: £ 1,046 Resection: £ 1,001 Patient £ 21.00 After 4 years: Health-care system: £ 1,231[j]	After 12 months: Health-care system: £ 1,315 Patient £ 73.40 After 4 years: Health-care system: £ 1,332	No data < 0.05 No data

[a] CG: Control group; EG: Experimental group.

[b] Per patient, including the costs associated with additional operations and with intraoperative and postoperative complications; mean value (± SD)(range).

[i] Health-care system resources used after 1994 discounted (rate of 6%) [Grant et al., 1999].

[j] Laser ablation or transcervical resection.

Table G (Cont'd)

Authors and year Country	Design	Participants	Treatments (n)[b]	Types of costs	Results[b]		
					Endometrial ablation	Hysterectomy	p
Ransom et al., 1996 United States	Retrospective Single-centre Follow-up of 2 months after the initial operation Hospital perspective, $US[d]	Menorrhagic women treated by endometrial ablation or hysterectomy between 1992 and 1994	CG: Abdominal (20) or vaginal (20) hysterectomy EG: Rollerball ablation (20)	Direct costs: Hospitalization[k], complications, additional operations	$3,765 US ($2,822 to $7,011 US)	Abdominal approach: $9,736 US ($6,792 to $12,890 US) Vaginal approach: $7,413 US ($4,188 to $12,028 US)	No data
Vilos et al., 1996a Canada	Retrospective Single-centre Follow-up of 12 months after the initial operation Societal perspective, 1995 $CDN	Menorrhagic women treated by endometrial ablation or vaginal hysterectomy between June 1992 and July 1993	CG: Vaginal hysterectomy (40) EG: Laser or rollerball ablation or transcervical resection (40)	Direct costs: Hospitalization[k], professional fees, anesthesia, additional operations Indirect costs: Lost productivity[l]	Direct costs: $2,174 CDN Indirect costs: $105 CDN	Direct costs: $4,231 CDN Indirect costs: $1,142 CDN	No data

[a] CG: Control group; EG: Experimental group.

[b] Per patient, including the costs associated with additional operations and with intraoperative and postoperative complications; mean value (± SD)(range).

[d] Year not specified.

[k] Determined by the hospital's finance department using standard methods for determining costs per activity.

[l] During convalescence; indirect costs = (length of convalescence) x (mean weekly salary) x (percentage of women in workforce in Ontario, Canada).

Table G (Cont'd)

Authors and year Country	Design	Participants	Treatments (n)[a]	Types of costs	Results[b]		
					Endometrial ablation	Hysterectomy	*P*
Hidlebaugh and Orr, 1998 United States	Retrospective Single-centre Follow-up of 36 months after the initial operation Societal perspective. $US[d]	Menorrhagic women treated by endometrial ablation between May 1992 and December 1994 or by hysterectomy between January 1990 and December 1992	CG: Abdominal (15), vaginal (15) or laparoscopically assisted vaginal (16) hysterectomy EG: Rollerball ablation (64)	Direct costs: Preoperative pharmacological thinning, related hospitalization costs, professional fees, anesthesia, complications, additional operations and medical consultations in gynecology during the 3 years following the initial operation Indirect costs: Lost productivity[h]	Direct costs: $5,434 US Indirect costs: $525 US	Direct costs[m]: $8,417 US Indirect costs[m]: $3,360 US Direct and indirect costs: Abdominal approach: $12,368 US Vaginal approach: $9,256 US Laparoscopically assisted vaginal approach: $13,365 US	< 0.001 < 0.001 No data

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[a] CG: Control group; EG: Experimental group.

[b] Per patient, including the costs associated with additional operations and with intraoperative and postoperative complications; mean value (± SD)(range).

[d] Year not specified.

[h] During convalescence; the indirect costs vary with the length of the convalescence, the workers' annual salary, the annual value of housework for women at home and the percentage of women in a given age group who are at home or in the workforce.

[m] Abdominal, vaginal or laparoscopically assisted vaginal hysterectomy.

Table G (Cont'd)

Authors and year Country	Design	Participants	Treatments (n)[a]	Types of costs	Results[b]		
					Endometrial ablation	Hysterectomy	P
Sculpher, 1998a United Kingdom	Cost-utility analysis, efficacy data taken from a randomized, controlled trial conducted by Dwyer et al. [1993] and from the long-term follow-up conducted by Sculpher et al. [1996] Decision tree equivalent to 2 years after the initial operation Health-care system perspective, 1994 £[n]	(See Sculpher et al., 1993) 60 menorrhagic women referred to a hospital between January and October 1994 because of various health problems	(See Sculpher et al., 1993)	(See Sculpher et al., 1993) Including the cost of screening by uterine smear	Estimated cost: £794 Estimated utility: 1.363 QALYs	Estimated cost: £1,139 Estimated utility: 1.593 QALYs Cost differential per additional QALY: £1,500	No data
London et al., 1999 United States	Retrospective Subjects followed for 12 months before and 12 months after the initial operation Third-party payer perspective, 1996 $US	Menometrorrhagic women covered by a health management organization, treated by endometrial ablation or hysterectomy between January 1996 and January 1998	CG: Abdominal (54) or laparoscopic (43) hysterectomy EG: Laser or rollerball ablation or transcervical resection (22)	Direct costs: Additional diagnostic examinations, medical consultations, medical treatment, preoperative pharmacological thinning, related hospitalization costs, anesthesia, professional fees, laboratory tests, drugs, complications, additional operations and medical consultations in gynecology during the 12 months following the initial operation	$4,927.67 US (± $2,900.85 US)	Abdominal approach: $9,231.15 US (± $3,958.93 US) Laparoscopic approach: $9,212.06 US (± $4,170.66 US)	Signif.[o] Signif.[o]

[a] CG: Control group; EG: Experimental group.

[b] Per patient, including the costs associated with additional operations and with intraoperative and postoperative complications; mean value (± SD)(range).

[n] All the health-care system resources used after the initial operation and the future QALYs were discounted (rate of 6%).

[o] Signif.: Significant; significance threshold = 0.1.

REFERENCES

Abenhaim HA, Dube D, Dufort J, Tulandi T. Cost analysis of laparoscopic hysterectomy, abdominal hysterectomy, and vaginal hysterectomy in a Canadian Teaching Hospital. J Obstet Gynaecol Can 2001;23:673-6.

Abramovich DR, Kitchener HC, Parkin DE, Lumsden MA, Scrimgeour JB, Duncan ID, et al. A Scottish audit of hysteroscopic surgery for menorrhagia: complications and follow up. Scottish Hysteroscopy Audit Group. Br J Obstet Gynaecol 1995;102:249-54.

Alaily A. Endometrial ablation with the Cavaterm thermal balloon. In: Hohl MK, Dequesne J, Eberhard M, editors. 7th Congress of the European Society for Gynaecological Endoscopy; December 6 to 9, 1998; Lausanne, Switzerland:17-20.

Aletebi FA, Vilos GA, Eskandar MA. Thermal balloon endometrial ablation to treat menorrhagia in high-risk surgical candidates. J Am Assoc Gynecol Laparosc 1999;6:435-9.

Alford WA, Hopkins MP. Endometrial rollerball ablation. J Reprod Med 1996;41:251-4.

Amso NN, Stabinsky SA, McFaul P, Blanc B, Pendley L, Neuwirth R. Uterine thermal balloon therapy for the treatment of menorrhagia: the first 300 patients from a multi-center study. International Collaborative Uterine Thermal Balloon Working Group. Br J Obstet Gynaecol 1998;105:517-23.

Baggish MS. Operative hysteroscopy. In: Thompson JD, Rock JA, editors. Te Linde's operative gynecology, 7th edition. Philadelphia: J.B. Lippincott Company, 1992:385-409.

Baggish M, Paraiso M, Breznock EM, Griffey S. A computer-controlled, continuously circulating, hot irrigating system for endometrial ablation. Am J Obstet Gynecol 1995;173:1842-8.

Baggish MS, Sze EHM. Endometrial ablation: a series of 568 patients treated over an 11-year period. Am J Obstet Gynecol 1996;174:908-13.

Bain C, Cooper KG, Parkin DE. A partially randomized patient preference trial of microwave endometrial ablation using local anaesthesia and intravenous sedation or general anaesthesia: a pilot study. Gynaecol Endosc 2001;10:223-8.

Bain C, Cooper KG, Parkin DE. Microwave endometrial ablation versus endometrial resection: a randomized controlled trial. Obstet Gynecol 2002;99:983-7.

Bernhard LA. Laser endometrial ablation: an alternative to hysterectomy. Health Care Women Int 1994;15:123-33.

Bhattacharya S, Cameron IM, Parkin De, Abramovich DR, Mollison J, Pinion SB, et al. A pragmatic randomised comparison of transcervical resection of the endometrium with endometrial laser ablation for the treatment of menorrhagia. Br J Obstet Gynaecol 1997;104:601-7.

Bongers MY, Mol BWJ, Brölmann HAM. Prognostic factors for the success of thermal balloon ablation in the treatment of menorrhagia. Obstet Gynecol 2002;99:1060-6.

Bongers MY, Mol BWJ, Dijkhuizen FPHLJ, Brölmann HAM. Is balloon ablation as effective as endometrial electroresection in the treatment of menorrhagia? J Laparoendosc Adv Surg Tech 2000;10:85-92.

Boujida VH, Philipsen T, Pelle J, Joergensen JC. Five-year follow-up of endometrial ablation: endometrial coagulation versus endometrial resection. Obstet Gynecol 2002;99:988-92.

Bridgman SA. Increasing operative rates for dysfunctional uterine bleeding after endometrial ablation. Lancet 1994;344:893.

Brooks PG, Clouse J, Stockwell Morris L. Hysterectomy versus resectoscopic endometrial ablation for the control of abnormal uterine bleeding: a cost-comparative study. J Reprod Med 1994;39:755-60.

Browne DS. Endometrial resection: a comparison of techniques. Aust N Z J Obstet Gynaecol 1996;36:448-52.

Brumsted JR, Blackman JA, Badger GJ, Riddick DH. Hysteroscopy versus hysterectomy for the treatment of abnormal uterine bleeding: a comparison of cost. Fertil Steril 1996; 65:310-6.

Brun JL, Geoffrion H, Harle T, Leng JJ. Thermocoagulation endométriale par ballonnet : technique, mécanisme d'action et évaluation. Gynecol Obstet Fertil 2000;28:303-8.

Buckshee K, Banerjee K, Bhatla H. Uterine balloon therapy to treat menorrhagia. Int J Gynaecol Obstet 1998;63:139-43.

Burke L, Rubin HW, Kim I. Uterine abscess formation secondary to endometrial cryosurgery. Obstet Gynecol 1973;41:224-6.

Bustos-Lopez HH, Baggish M, Valle RF, Vadillo-Ortega F, Ibarra V, Nava G. Assessment of the safety of intrauterine instillation of heated saline for endometrial ablation. Fertil Steril 1998;69:155-60.

Cahan WG, Brockunier A Jr. Cryosurgery of the uterine cavity. Am J Obstet Gynecol 1967;99:138-53.

Cameron IM, Mollison J, Pinion SB, Atherton-Naji A, Buckingham K, Torgerson D. A cost comparison of hysterectomy and hysteroscopic surgery for the treatment of menorrhagia. Eur J Obstet Gynecol Reprod Biol 1996;70:87-92.

Chullapram T, Song JY, Fraser IS. Medium-term follow-up of women with menorrhagia treated by rollerball endometrial ablation. Obstet Gynecol 1996;88:71-6.

Conseil d'évaluation des technologies de la santé du Québec (CETS). Le traitement chirurgical de l'obésité morbide. Montréal: CETS; 1998.

Cooke I, Lethaby A, Farquhar C. Antifibrinolytics for heavy menstrual bleeding (Cochrane Review). The Cochrane Library, Issue 4, 2000. Oxford: Update Software.

Cooper JM, Brady RM. Gynecologic operative endoscopy. Hysteroscopy in the management of abnormal uterine bleeding. Obstet Gynecol Clin North Am 1999;26:217-36.

Cooper JM, Erickson ML. Global endometrial ablation technologies. Obstet Gynecol Clin North Am 2000;27:385-96.

Cooper KG, Bain C, Parkin DE. Comparison of microwave endometrial ablation and transcervical resection of the endometrium for treatment of heavy menstrual loss: a randomised trial. Lancet 1999a;354:1859-63.

Cooper KG, Parkin DE, Garratt AM, Grant AM. A randomised comparison of medical and hysteroscopic management in women consulting a gynaecologist for treatment of heavy menstrual loss. Br J Obstet Gynaecol 1997;104:1360-6.

Cooper KG, Parkin DE, Garratt AM, Grant AM. Two-year follow up of women randomised to medical management or transcervical resection of the endometrium for heavy menstrual loss: clinical and quality of life outcomes. Br J Obstet Gynaecol 1999b;106:258-65.

Corson SL. A multicenter evaluation of endometrial ablation by Hydro ThermAblator and rollerball for treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2001;8:359-67.

Corson SL, Brill AI, Brooks PG, Cooper JM, Indman PD, Liu JH, et al. Interim results of the American Vesta Trial of endometrial ablation. J Am Assoc Gynecol Laparosc 1999;6:45-9.

Corson SL, Brill AI, Brooks PG, Cooper JM, Indman PD, Liu JH, et al. One-year results of the American Vesta Trial for endometrial ablation. J Am Assoc Gynecol Laparosc 2000;7:489-97.

Coulter A, Kelland J, Peto V, Rees MCP. Treating menorrhagia in primary care: an overview of drug trials and a survey of prescribing practice. Int J Technol Assess Health Care 1995;11:456-71.

Crosignani PG, Vercellini P, Apolone G, De Giorgi O, Cortesi I, Meschia M. Endometrial resection versus vaginal hysterectomy for menorrhagia: long-term clinical and quality-of-life outcomes. Am J Obstet Gynecol 1997a;177:95-101.

Crosignani PG, Vercellini P, Mosconi P, Oldani S, Cortesi I, De Giorgi O. Levonorgestrel-releasing intrauterine device versus hysteroscopic endometrial resection in the treatment of dysfunctional uterine bleeding. Obstet Gynecol 1997b;90:257-63.

Cucherat M. Méta-analyse des essais thérapeutiques. Paris: Masson; 1997.

Daniell JF, Kurtz BR, Lee RW. Hysteroscopic endometrial ablation using the rollerball electrode. Obstet Gynecol 1992;80:329-32.

das Dores GB, Richart RM, Nicolau SM, Focchi GR, Cordeiro VC. Evaluation of Hydro ThermAblator for endometrial destruction in patients with menorrhagia. J Am Assoc Gynecol Laparosc 1999;6:275-8.

Davis JR, Maynard KK, Brainard CP, Purdon TF, Sibley MA, King DD. Effects of thermal endometrial ablation: clinicopathologic correlations. Am J Clin Pathol 1998;109:96-100.

DeCherney AH, Diamond MP, Lavy G, Polan ML. Endometrial ablation for intractable uterine bleeding: hysteroscopic resection. Obstet Gynecol 1987;70:668-70.

De Grandi P, El Din A. Endometrial ablation for the treatment of dysfunctional uterine bleeding using balloon therapy. Contrib Gynecol Obstet 2000;20:145-53.

Dequesne J, Gallinat A, Garza-Leal JG, Sutton CF, van der Pas HF, Wamsteker K, et al. Thermoregulated radiofrequency endometrial ablation. Int J Fertil 1997;42:311-8.

Dicker RC, Greenspan JR, Strauss LT, Cowart MR, Scally MJ, Peterson HB, et al. Complications of abdominal and vaginal hysterectomy among women of reproductive age in the United States. The Collaborative Review of Sterilization. Am J Obstet Gynecol 1982;144:841-8.

Dobak J, Ryba E, Kovalcheck S. A new closed-loop cryosurgical device for endometrial ablation. J Am Assoc Gynecol Laparosc 2000a;7:245-9.

Dobak JD, Willems J. Extirpated uterine endometrial cryoablation with ultrasound visualization. J Am Assoc Gynecol Laparosc 2000;7:95-101.

Dobak JD, Willems J, Howard R, Shea C, Townsend DE. Endometrial cryoablation with ultrasound visualization in women undergoing hysterectomy. J Am Assoc Gynecol Laparosc 2000b;7:89-93.

Donnez J, Polet R, Rabinovitz R, Ak M, Squifflet J, Nisolle M. Endometrial laser intrauterine thermotherapy: the first series of 100 patients observed for 1 year. Fertil Steril 2000; 74:791-6.

Droegemueller W, Greer BE, Makowski EL. Preliminary observations of cryocoagulation of the endometrium. Am J Obstet Gynecol 1970;107:958-61.

Droegemueller W, Greer B, Makowski E. Cryosurgery in patients with dysfunctional uterine bleeding. Obstet Gynecol 1971a;38:256-8.

Droegemueller W, Greer B, Makowski E. Destruction of the endometrium by cryosurgery. Am J Obstet Gynecol 1971b;110:467-9.

Droegemueller W, Greer BE, Davis JR, Makowski EL, Chvapil M, Pollard A. Cryocoagulation of the endometrium at the uterine cornua. Am J Obstet Gynecol 1978; 131:1-9.

Dutton C, Ackerson L, Phelps-Sandall B. Outcomes after rollerball endometrial ablation for menorrhagia. Obstet Gynecol 2001;98:35-9.

Dwyer N, Hutton J, Stirrat GM. Randomised controlled trial comparing endometrial resection with abdominal hysterectomy for the surgical treatment of menorrhagia. Br J Obstet Gynaecol 1993;100:237-43.

Ellstrom M, Ferraz-Nunes J, Hahlin M, Olsson JH. A randomized trial with a cost-consequence analysis after laparoscopic and abdominal hysterectomy. Obstet Gynecol 1998;91:30-4.

El Senoun GSA, Mousa HA, Mahmood TA. Medium-term follow-up of women with menorrhagia treated by rollerball endometrial ablation. Acta Obstet Gynecol Scand 2000;79:879-83.

Erian J. Endometrial ablation in the treatment of menorrhagia. Br J Obstet Gynaecol 1994;101(suppl 11):19-22.

Everett RB. Five-year review of endometrial ablation with the SideFire Laser Fiber. J Am Assoc Gynecol Laparosc 1999;6:65-9.

Fehr M, Geissbuehler V, Eberhard J. The hydrothermablation (HTA) in local anaesthesia. In: Hohl MK, Dequesne J, Eberhard M, editors. 7th Congress of the European Society for Gynaecological Endoscopy; December 6 to 9, 1998; Lausanne,Switzerland: 145-7.

Fernandez H, Capella S, Audibert F. Uterine thermal balloon therapy under local anaesthesia for the treatment of menorrhagia: a pilot study. Hum Reprod 1997;12:2511-4.

Floridon C, Lund N, Thomsen SG. Alternative treatment for symptomatic fibroids. Curr Opin Obstet Gynecol 2001;13:491-5.

Food and Drug Administration (FDA). PMA P970021: Summary of safety and effectiveness data: ThermaChoice™ Uterine Balloon Therapy™ System. Rockville: FDA, 1997. Available at: http://www.fda.gov/cdrh/pdf/p970021.pdf (consulted on February 6, 2001).

Food and Drug Administration (FDA). PMA P000032: Approval order. HerOption™ Uterine Cryoblation Therapy™ System. Rockville: FDA, 2001a. Available at http://www.fda.gov/cdrh/pdf/p000032a.pdf (consulted on May 9, 2001).

Food and Drug Administration (FDA). PMA P000032: Summary of safety and effectiveness data: HerOption™ Uterine Cryoblation Therapy™ System. Rockville: FDA, 2001b. Available at: http://www.fda.gov/cdrh/pdf/p000032b.pdf (consulted on February 6, 2002).

Food and Drug Administration (FDA). PMA P000040: Approval order. Hydro ThermAblator® Endometrial Ablation System. Rockville: FDA, 2001c. Available at: http://www.fda.gov/cdrh/pdf/p000040a.pdf (consulted on May 9, 2001).

Food and Drug Administration (FDA). PMA P000040: Summary of safety and effectiveness data. Hydro ThermAblator® Endometrial Ablation System. Rockville: FDA, 2001d. Available at http://www.fda.gov/cdrh/pdf/p000040b.pdf (consulted on February 6, 2002).

Food and Drug Administration (FDA). PMA P010013: Approval order. NovaSure™ Impedance Controlled Endometrial Ablation System. Rockville: FDA, 2001e. Available at http://www.fda.gov/cdrh/pdf/p010013a.pdf (consulted on March 28, 2002).

Food and Drug Administration (FDA). PMA P010013: Summary of safety and effectiveness data: NovaSure™ Impedance Controlled Endometrial Ablation System. Rockville: FDA, 2001f. Available at http://www.fda.gov/cdrh/pdf/p010013b.pdf (consulted on March 28, 2002).

Fraser IS, Angsuwathana S, Mahmoud F, Yezerski S. Short and medium term outcomes after rollerball endometrial ablation for menorrhagia. Med J Aust 1993;158:444-7.

Fraser IS, Healy DL, Torode H, Song JY, Mamers P, Wilde F. Depot goserelin and danazol pretreatment before rollerball endometrial ablation for menorrhagia. Obstet Gynecol 1996;87:544-50.

Friberg B, Ahlgren M. Cavaterm™ endometrial ablation, results at 5 years follow-up. In: Hohl MK, Dequesne J, Eberhard M, editors. 7th Congress of the European Society for Gynaecological Endoscopy; December 6 to 9, 1998; Lausanne, Switzerland:31-4.

Friberg B, Ahlgren M. Thermal balloon endometrial destruction: the outcome of treatment of 117 women followed up for a maximum period of 4 years. Gynaecol Endosc 2000; 9:389-95.

Friberg B, Persson BRR, Willén R, Ahlgren M. Endometrial destruction by thermal coagulation: evaluation of a new form of treatment for menorrhagia. Gynaecol Endosc 1998;7:73-8.

Gallinat A. Endometrial ablation by balloon coagulation. Contrib Gynecol Obstet 2000;20:137-44.

Gallinat A, Cosgriff N. Endometrial ablation by electroballoon coagulation: long-term results. Gynaecol Endosc 2001;10:37-43.

Gannon MJ, Holt EM, Fairbank J, Fitzgerald M, Milne MA, Crystal AM, et al. A randomised trial comparing endometrial resection and abdominal hysterectomy for the treatment of menorrhagia. BMJ 1991;303:1362-4.

Gannon MJ, Day P, Hammadieh N, Johnson N. A new method of measuring menstrual blood loss and its use in screening women before endometrial ablation. Br J Obstet Gynaecol 1996;103:1029-33.

Garry R. Endometrial ablation vs laparoscopic hysterectomy. Pro endometrial ablation. J Gynecol Surg 1995a;11:57-8.

Garry R. Good practice with endometrial ablation. Obstet Gynecol 1995b;85:144-51.

Garry R, Erian J, Grochmal SA. A multicentre collaborative study into the treatment of menorrhagia by Nd-YAG laser ablation of the endometrium. Br J Obstet Gynaecol 1991;98:357-62.

Garry R, Phillips G. How safe is the laparoscopic approach to hysterectomy? Gynaecol Endosc 1995;4:77-9.

Garry R, Shelley-Jones D, Mooney P, Phillips G. Six hundred endometrial laser ablations. Obstet Gynecol 1995;85:24-9.

Genolet PM, Gerber S, De Grandi P, Friberg B, Ahlgren M. Endometrial ablation for dysfunctional uterine bleeding in the perimenopause, clinical results of a multicentre trial with the Cavaterm™ thermal balloon. In: Aso T, Yanaihara T, Taketani Y, Suda T, Tanaka H, Maehara S, editors. 9th International Menopause Society World Congress on the Menopause; October 17 to 21, 1999; Yokohama, Japan:315-20.

Gervaise A, Fernandez H, Capella-Allouc S, Taylor S, Vieille SL, Hamou J, et al. Thermal balloon ablation versus endometrial resection for the treatment of abnormal uterine bleeding. Hum Reprod 1999;14:2743-7.

Gimpelson RJ. Hysteroscopic Nd:YAG laser ablation of the endometrium. J Reprod Med 1988;33:872-6.

Goldfarb HA. A review of 35 endometrial ablations using the Nd:YAG laser for recurrent menometrorrhagia. Obstet Gynecol 1990;76:833-5.

Goldrath MH. Use of danazol in hysteroscopic surgery for menorrhagia. J Reprod Med 1990;35:91-6.

Goldrath MH, Barrionuevo M, Husain M. Endometrial ablation by hysteroscopic instillation of hot saline solution. J Am Assoc Gynecol Laparosc 1997;4:235-40.

Goldrath MH, Fuller TA, Seqal S. Laser photovaporization of endometrium for the treatment of menorrhagia. Am J Obstet Gynecol 1981;140:14-9.

Grainger DA, Tjaden BL, Rowland C, Meyer WR. Thermal balloon and rollerball ablation to treat menorrhagia: two-year results of a multicenter, prospective, randomized, clinical trial. J Am Assoc Gynecol Laparosc 2000;7:175-9.

Grant AM, Bhattacharya S, Mollison J, McIntosh E. A randomised trial of endometrial ablation versus hysterectomy for the treatment of dysfunctional uterine bleeding: outcome at four years. Aberdeen Endometrial Ablation Trials Group. Br J Obstet Gynaecol 1999; 106:360-6.

Grant C, Gallier L, Fahey T, Pearson N, Sarangi J. Management of menorrhagia in primary care: impact on referral and hysterectomy: data from the Somerset Morbidity Project. J Epidemiol Community Health 2000;54:709-13.

Hawe JA, Phillips AG, Chien PFW, Erian J, Garry R. Cavaterm thermal balloon ablation for the treatment of menorrhagia. Br J Obstet Gynaecol 1999;106:1143-8.

Health Technology Advisory Committee (HTAC). Surgical alternatives to hysterectomy for abnormal uterine bleeding. Minnesota Health Technology Advisory Committee: June 2000. Available at: http://www.health.state.mn.us/htac/sah.htm.

Heppard M, Coddington C, Duleba A, Soderstrom R, Townsend D, Willems J. Data on 222 patients from a multicenter study using Cryogen First Option Uterine Cryoblation Therapy in women with abnormal uterine bleeding [abstract]. Obstet Gynecol 2001;97(4 suppl 1):21S.

Hidlebaugh DA. Cost and quality-of-life issues associated with different surgical therapies for the treatment of abnormal uterine bleeding. Obstet Gynecol Clin North Am 2000;27:451-65.

Hidlebaugh DA. Relative costs of gynecologic endoscopy vs traditional surgery for treatment of abnormal uterine bleeding. Am J Manag Care 2001;7:SP31-SP37.

Hildlebaugh DA, Orr RK. Long-term economic evaluation of resectoscopic endometrial ablation versus hysterectomy for the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 1998;5:351-6.

Higham JM, O'Brien PMS, Shaw RW. Assessment of menstrual blood loss using a pictorial chart. Br J Obstet Gynaecol 1990;97:734-9.

Hirsch NA. Diffusion and cost considerations for minimally invasive techniques in gynaecology. Minim Invasive Ther 1994;3:343-9.

Hodgson DA, Feldberg IB, Sharp N, Cronin N, Evans M, Hirschowitz L. Microwave endometrial ablation: development, clinical trial and outcomes at three years. Br J Obstet Gynaecol 1999;106:684-94.

Holt EM, Gillmer MDG. Endometrial resection. Baillieres Clin Obstet Gynaecol 1995;9: 279-97.

Hullberg L, Hogdahi AM, Nilsson L, Rybo G. Menstrual blood loss: a population study. Acta Obstet Gynecol Scand 1966;45:320-51.

Hurskainen R, Aalto A, Teperi J, Grenman S, Kivela A, Kujansuu F, Vuorma, et al. Psychosocial and other characteristics of women complaining of menorrhagia, with and without actual increased menstrual blood loss. Br J Obstet Gynaecol 2001;108:281-5.

Istre O, Trolle B. Treatment of menorrhagia with the levonorgestrel intrauterine system versus endometrial resection. Fertil Steril 2001;76:304-9.

Iyer V, Farquhar C, Jepson R. Oral contraceptive pills for heavy menstrual bleeding (Cochrane Review). The Cochrane Library, Issue 4, 2000. Oxford: Update Software.

Jansen FW, Vredevoogd CB, Van Ulzen K, Hermans J, Trimbos JB, Trimbos-Kemper TCM. Complication of hysteroscopy: a prospective, multicenter study. Obstet Gynecol 2000;96:266-70.

Janssen CAH, Scholten PC, Heintz APM. A simple visual assessment technique to discriminate between menorrhagia and normal menstrual blood loss. Obstet Gynecol 1995;85:977-82.

Jones K, Abbott J, Hawe J, Sutton C, Garry R. Endometrial laser intrauterine thermotherapy for the treatment of dysfunctional uterine bleeding: the first British experience. Br J Obstet Gynaecol 2001;108:749-53.

Jones KD, McGurgan P, Sutton CJG. Second-generation endometrial ablation techniques. Curr Opin Obstet Gynecol 2000;12:273-6.

Kammerer-Doak DN, Rogers RG. Endometrial ablation: electrocautery and laser techniques. Clin Obstet Gynecol 2000;43:561-74.

Ke RW. Endometrial ablation: an alternative to hysterectomy. Clin Obstet Gynecol 1997; 40:914-27.

Kelleher C, Braude P. Recent advances. Gynaecology. BMJ 1999;319(7211):689-92.

Korn AP. Endometrial cryoablation and thermal ablation. Clin Obstet Gynecol 2000; 43:575-83.

Kovac SR, Christie SJ, Bindbeutel GA. Abdominal versus vaginal hysterectomy: a statistical model for determining physician decision making and patient outcome. Med Decis Making 1991;11:19-28.

Kriplani A, Manchanda R, Nath J, Takkar D. A randomized trial of danazol pretreatment prior to endometrial resection. Eur J Obstet Gynecol Reprod Biol 2002;103:68-71.

Kumar S, Suneetha PV, Dadhwal V, Mittal S. Endometrial cryoablation in the treatment of dysfunctional uterine bleeding. Int J Gynaecol Obstet 2002;76:189-90.

Laupacis A, Feeny D, Detsky A, Tugwell PX. How attractive does a new technology have to be to warrant adoption and utilization? Tentative guidelines for using clinical and economic evaluation. Can Med Assoc J 1992;146:473-81.

Lethaby A, Augood C, Duckitt K. Nonsteroidal anti-inflammatory drugs for heavy menstrual bleeding (Cochrane Review). The Cochrane Library, Issue 4, 2000a. Oxford: Update Software.

Lethaby A, Cooke I, Rees M. Progesterone/progestogen releasing intrauterine systems versus either placebo or any other medication for heavy menstrual bleeding (Cochrane Review). The Cochrane Library, Issue 4, 2000b. Oxford: Update Software.

Lethaby A, Hickey M. Endometrial destruction techniques for heavy menstrual bleeding (Protocol for a Cochrane Review). The Cochrane Library, Issue 1, 2001. Oxford: Update Software.

Lethaby A, Hickey M. Endometrial destruction techniques for heavy menstrual bleeding (Cochrane Review). The Cochrane Library, Issue 2, 2002. Oxford: Update Software.

Lethaby A, Irvine G, Cameron I. Cyclical progestogens for heavy menstrual bleeding. (Cochrane Review). The Cochrane Library, Issue 4, 2000c. Oxford: Update Software.

Lethaby A, Shepperd S, Cooke I, Farquhar C. Endometrial resection and ablation versus hysterectomy for heavy menstrual bleeding (Cochrane Review). The Cochrane Library, Issue 4, 2000d. Oxford: Update Software.

Lissak A, Fruchter O, Mashiach S, Brandes-Klein O, Haron A, Kogan O, et al. Immediate versus delayed treatment of perimenopausal bleeding due to benign causes by balloon thermal ablation. J Am Assoc Gynecol Laparosc 1999;6:145-50.

Loffer FD. Three-year comparison of thermal balloon and rollerball ablation in treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2001;8:48-54.

Lomano JM, Feste JR, Loffer FD, Goldrath MH. Ablation of the endometrium with the neodymium: YAG laser: a multicenter study. Colposc Gynecol Laser Surg 1986;2:203-7.

London R, Holzman M, Rubin D, Moffitt B. Payer cost savings with endometrial ablation therapy. Am J Manag Care 1999;5:889-97.

Luukkainen T. The levonorgestrel intrauterine system: therapeutic aspects. Steroids2000;65: 699-702.

Machan L, Martin M. Uterine artery embolization to treat uterine fibroids. Can Assoc Radiol J 2001;52:183-7.

MacLean-Fraser E, Penava D, Vilos GA. Perioperative complication rates of primary and repeat hysteroscopic endometrial ablations. J Am Assoc Gynecol Laparosc 2002;9:175-7.

Magos AL, Baumann R, Lockwood GM, Turnbull AC. Experience with the first 250 endometrial resections for menorrhagia. Lancet 1991;337:1074-8.

Maher PJ, Hill DJ. Transcervical endometrial resection for abnormal uterine bleeding: report of 100 cases and review of the literature. Aust N Z J Obstet Gynaecol 1990;30:357-60.

McCausland AM, McCausland VM. Intrauterine scarring as a result of total endometrial ablation could delay the diagnosis of endometrial cancer. Am J Obstet Gynecol 1999a;180:1598-9.

McCausland AM, McCausland VM. Partial rollerball endometrial ablation: a modification of total ablation to treat menorrhagia without causing complications from intrauterine adhesions. Am J Obstet Gynecol 1999b;180:1512-21.

Medical Devices Agency (MDA). Devices used for endometrial ablation achieved by thermal means. Safety Notice 1998 March; MDA SN 9812.

Medical Devices Agency (MDA). Devices used for endometrial ablation. Safety Notice 1999 May; MDA SN 1999(18).

Meyer WR, Walsh BW, Grainger DA, Peacock LM, Loffer FD, Steege JF. Thermal balloon and rollerball ablation to treat menorrhagia: a multicenter comparison. Obstet Gynecol 1998;92:98-103.

Millar WJ. Hysterectomy, 1981-1982 to 1996-1997. Health Reports February 2001; 12:9-24. (Statistics Canada, No. 82-003 in the catalogue).

Milligan MP, Etokowo GA. Microwave endometrial ablation for menorrhagia. J Obstet Gynaecol 1999;19:496-9.

Mousa HA, El Senoun GMSA, Mahmood TA. Medium-term clinical outcome of women with menorrhagia treated by rollerball endometrial ablation versus abdominal hysterectomy with conservation of at least one ovary. Acta Obstet Gynecol Scand 2001;80:442-6.

Nagele F, Rubinger T, Magos A. Why do women choose endometrial ablation rather than hysterectomy? Fertil Steril 1998;69:1063-6.

NHS Centre for Reviews and Dissemination (NHSCRD). The management of menorrhagia. What are effective ways of treating excessive regular menstrual blood loss in primary and secondary care? Effect Health Care Bull 1995;9:15 pages.

O'Connor H, Broadbent JA, Magos AL, McPherson K. Medical Research Council randomised trial of endometrial resection versus hysterectomy in management of menorrhagia. Lancet 1997;349:897-901.

O'Connor H, Magos A. Endometrial resection for the treatment of menorrhagia. N Engl J Med 1996;335:151-6.

Overton C, Hargreaves H, Maresh M. A national survey of the complications of endometrial destruction for menstrual disorders: the MISTLETOE study. Br J Obstet Gynaecol 1997;104:1351-9.

Parkin DE. Prognostic factors for success of endometrial ablation and resection. Lancet 1998;351:1147-8.

Parkin DE. Endometrial resection and ablation: past, present and future. Gynaecol Endosc 2000a;9:1-7.

Parkin DE, for the MEA™ Users' Group. Microwave endometrial ablation (MEA™): a safe technique? Complication data from a prospective series of 1400 cases. Gynaecol Endosc 2000b;9:385-8.

Paskowitz RA. Rollerball ablation of the endometrium. J Reprod Med 1995;40:333-6.

Perlitz Y, Rahav D, Ben-Ami M. Endometrial ablation using hysteroscopic instillation of hot saline solution into the uterus. Eur J Obstet Gynecol Reprod Biol 2001;99:90-2.

Perry CP, Daniell JF, Gimpelson RJ. Bowel injury from Nd: YAG endometrial ablation. J Gynecol Surg 1990;6:199-203.

Phillips DR. A comparison of endometrial ablation using the Nd: YAG laser or electrosurgical techniques. J Am Assoc Gynecol Laparosc 1994;1:235-9.

Phillips G, Chien PFW, Garry R. Risk of hysterectomy after 1000 consecutive endometrial laser ablations. Br J Obstet Gynaecol 1998;105:897-903.

Pinion SB, Parkin DE, Abramovich DR, Naji A, Alexander DA, Russell IT, et al. Randomised trial of hysterectomy, endometrial laser ablation, and transcervical endometrial resection for dysfunctional uterine bleeding. BMJ 1994;309:979-83.

Pittrof R, Majid S, Murray A. Transcervical endometrial cryoablation (ECA) for menorrhagia. Int J Gynaecol Obstet 1994;47:135-40.

Prentice A. Medical management of menorrhagia. BMJ 1999;319:1343-5.

Propst AM, Liberman RF, Harlow BL, Ginsburg ES. Complications of hysteroscopic surgery: predicting patients at risk. Obstet Gynecol 2000;96:517-20.

Pyper RJ, Haeri AD. A review of 80 endometrial resections for menorrhagia. Br J Obstet Gynaecol 1991;98(10):1049-54.

Rai VS, Gillmer MDG, Gray W. Is endometrial pre-treatment of value in improving the outcome of transcervical resection of the endometrium? Hum Reprod 2000; 15:1989-92.

Rankin L, Steingerg LH. Transcervical resection of the endometrium: a review of 400 consecutive patients. Br J Obstet Gynaecol 1992;99:911-4.

Ransom SB, McNeeley SG, White C, Diamond MP. A cost analysis of endometrial ablation, abdominal hysterectomy, vaginal hysterectomy, and laparoscopic-assisted vaginal hysterectomy in the treatment of primary menorrhagia. J Am Assoc Gynecol Laparosc 1996;4:29-32.

Richart RM, das Dores GB, Nicolau SM, Focchi GR, Cordeiro VC. Histologic studies of the effects of circulating hot saline on the uterus before hysterectomy. J Am Assoc Gynecol Laparosc 1999;6:269-73.

Römer T, Müller J. A simple method of coagulating endometrium in patients with therapy-resistant, recurring hypermenorrhea. J Am Gynecol Laparosc 1999;6:265-8.

Römer T, Müller J, Foth D. Hydrothermal ablation. A new simple method for coagulating endometrium in patients with therapy-resistant recurring hypermenorrhea. Contrib Gynecol Obstet 2000;20:154-60.

Ruta DA, Garratt AM, Chadha YC, Flett GM, Hall MH, Russell IT. Assessment of patients with menorrhagia: how valid is a structured clinical history as a measure of health status? Qual Life Res 1995;4:33-40.

Rutherford TJ, Zreik TG, Troiano RN, Palter SF, Olive DL. Endometrial cryoablation, a minimally invasive procedure for abnormal uterine bleeding. J Am Assoc Gynecol Laparosc 1998;5:23-8.

Salat-Baroux J, Hamou J, Antoine JM. La résection hystéroscopique de l'endomètre : une alternative à l'hystérectomie ? Bull Acad Natl Med 1996;180:2139-47.

Sanders B. Preliminary outcomes of longer freeze cycles in the treatment of women with abnormal uterine bleeding using CryoGen First Option Uterine Cryoblation Therapy [abstract]. Obstet Gynecol 2001;97(4 suppl 1):14S.

Sculpher M. A cost-utility analysis of abdominal hysterectomy versus transcervical endometrial resection for the surgical treatment of menorrhagia. Int J Technol Assess Health Care 1998a;14:302-19.

Sculpher M. The cost-effectiveness of preference-based treatment allocation: the case of hysterectomy versus endometrial resection in the treatment of menorrhagia. Health Econ 1998b;7:129-42.

Sculpher MJ, Bryan S, Dwyer N, Hutton J, Stirrat GM. An economic evaluation of transcervical endometrial resection versus abdominal hysterectomy for the treatment of menorrhagia. Br J Obstet Gynaecol 1993;100:244-52.

Sculpher MJ, Dwyer N, Byford S, Stirrat GM. Randomised trial comparing hysterectomy and transcervical endometrial resection: effect on health related quality of life and cost two years after surgery. Br J Obstet Gynaecol 1996;103:142-9.

Serden SP, Brooks PG. Treatment of abnormal uterine bleeding with the gynecologic resectoscope. J Reprod Med 1991;36:697-9.

Sharp NC, Cronin N, Feldberg I, Evans M, Hodgson D, Ellis S. Microwaves for menorrhagia: a new fast technique for endometrial ablation. Lancet 1995;346:1003-4.

Sharp NC, Feldberg IB, Hodgson DA, Butters B, Cronin N. Microwave Endometrial Ablation. In: Sutton C, Diamond MP, editors. Endoscopic Surgery for Gynaecologists, 2nd edition. London: WB Saunders Company Ltd; 1998:630-7.

Sharp N, Hodgson DA, Ellard MA, Feldberg I. Microwave endometrial ablation: prospective study covering 4 years experience of over 300 patients. Alternatives to hysterectomy: proceedings from the World Congress on Hysteroscopy (The American Association of Gynecologic Laparoscopists); February 25 to 27, 2000; Miami Beach, Florida.

Simon NV, Laveran RL, Cavanaugh S, Gerlach DH, Lackson JR. Laparoscopic supracervical hysterectomy vs abdominal hysterectomy in a community hospital: a cost comparison. J Reprod Med 1999;44:339-45.

Singer A, Almanza R, Gutierrez A, Haber G, Bolduc LR, Neuwirth R. Preliminary clinical experience with a thermal balloon endometrial ablation method to treat menorrhagia. Obstet Gynecol 1994;83:732-4.

Snowden R, Christian B. Patterns and perceptions of menstruation: a World Health Organization international collaborative study in Egypt, India, Indonesia, Jamaica, Mexico, Pakistan, Philippines, Republic of Korea, United Kingdom and Yugoslavia. London: Croom Helm; 1983.

Sowter MC, Singla AA, Lethaby A. Pre-operative endometrial thinning agents before hysteroscopic surgery for heavy menstrual bleeding (Cochrane Review). The Cochrane Library, Issue 4, 2000. Oxford: Update Software.

Speroff L, Glass RH, Kase NG. Dysfunctional uterine bleeding. In: Speroff L, Glass RH, Kase NG, editors. Clinical gynecologic endocrinology and fertility. 6th edition. Baltimore: Lippincott Williams & Wilkins, 1999:575-93.

Steffensen AJ, Schuster M. Endometrial resection and late reoperation in the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 1997;4:325-9.

Swartz DP, Butler WJ. Normal and abnormal uterine bleeding. In: Thompson JD, Rock JA, editors. Te Linde's operative gynecology. 7th edition. Philadelphia: J.B. Lippincott Company, 1992:297-316.

Sylvestre C, Laberge PY, Bazin S, Bérubé S. Incidence cumulative d'hystérectomies chez les femmes ayant subi une résection hystéroscopique de l'endomètre. J Obstet Gynaecol Can 2000;22:192-9.

Teirney R, Arachchi GJ, Fraser IS. Menstrual blood loss measured 5-6 years after endometrial ablation. Obstet Gynecol 2000;95:251-4.

Tulandi T. Microwaves: from the kitchen to the operating theatre. CMAJ 1999;161:1132.

Tulandi T, Felemban A. Hysteroscopic appearance of the uterine cavity before and after microwave endometrial ablation. J Am Assoc Gynecol Laparosc 2001;8:83-6.

Ulmsten U, Carstensen H, Falconer C, Holm L, Lanner L, Nilsson S, et al. The safety and efficacy of MenoTreat™, a new balloon device for thermal endometrial ablation. Acta Obstet Gynecol Scand 2001;80:52-7.

Unger JB, Meeks GR. Hysterectomy after endometrial ablation. Am J Obstet Gynecol 1996;175:1432-7.

Valle RF. Rollerball endometrial ablation. Baillieres Clin Obstet Gynaecol 1995;9:299-316.

Vancaillie TG. Electrocoagulation of the endometrium with the ball-end resectoscope. Obstet Gynecol 1989;74:425-7.

Varol N, Healey M, Tang P, Sheehan P, Maher P, Hill D. Ten-year review of hysterectomy morbidity and mortality: can we change direction? Aust N Z J Obstet Gynaecol 2001;41:295-302.

Vilos GA, Aletebi FA, Eskandar MA. Endometrial thermal balloon ablation with the ThermaChoice system: effect of intrauterine pressure and duration of treatment. J Am Assoc Gynecol Laparosc 2000;7:325-9.

Vilos GA, D'Souza I, Huband D. Genital tract burns during rollerball endometrial coagulation. J Am Assoc Gynecol Laparosc 1997a;4:273-6.

Vilos GA, Fortin CA, Sanders B, Pendley L, Stabinsky SA. Clinical trial of the uterine thermal balloon for the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 1997b;4:559-65.

Vilos GA, Lefebvre G, Graves GR. Lignes directrices sur la prise en charge du saignement utérin anormal. J Obstet Gynaecol Can 2001;23:710-6.

Vilos GA, Pispidikis JT, Botz CK. Economic evaluation of hysteroscopic endometrial ablation versus vaginal hysterectomy for menorrhagia. Obstet Gynecol 1996a;88:241-5.

Vilos GA, Vilos EC, King JH. Experience with 800 hysteroscopic endometrial ablations. J Am Assoc Gynecol Laparosc 1996b;4:33-8.

Vilos GA, Vilos EC, Pendley L. Endometrial ablation with a thermal balloon for the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 1996c;3:383-7.

Weber AM. Endometrial ablation. Obstet Gynecol 2002;99:969-70.

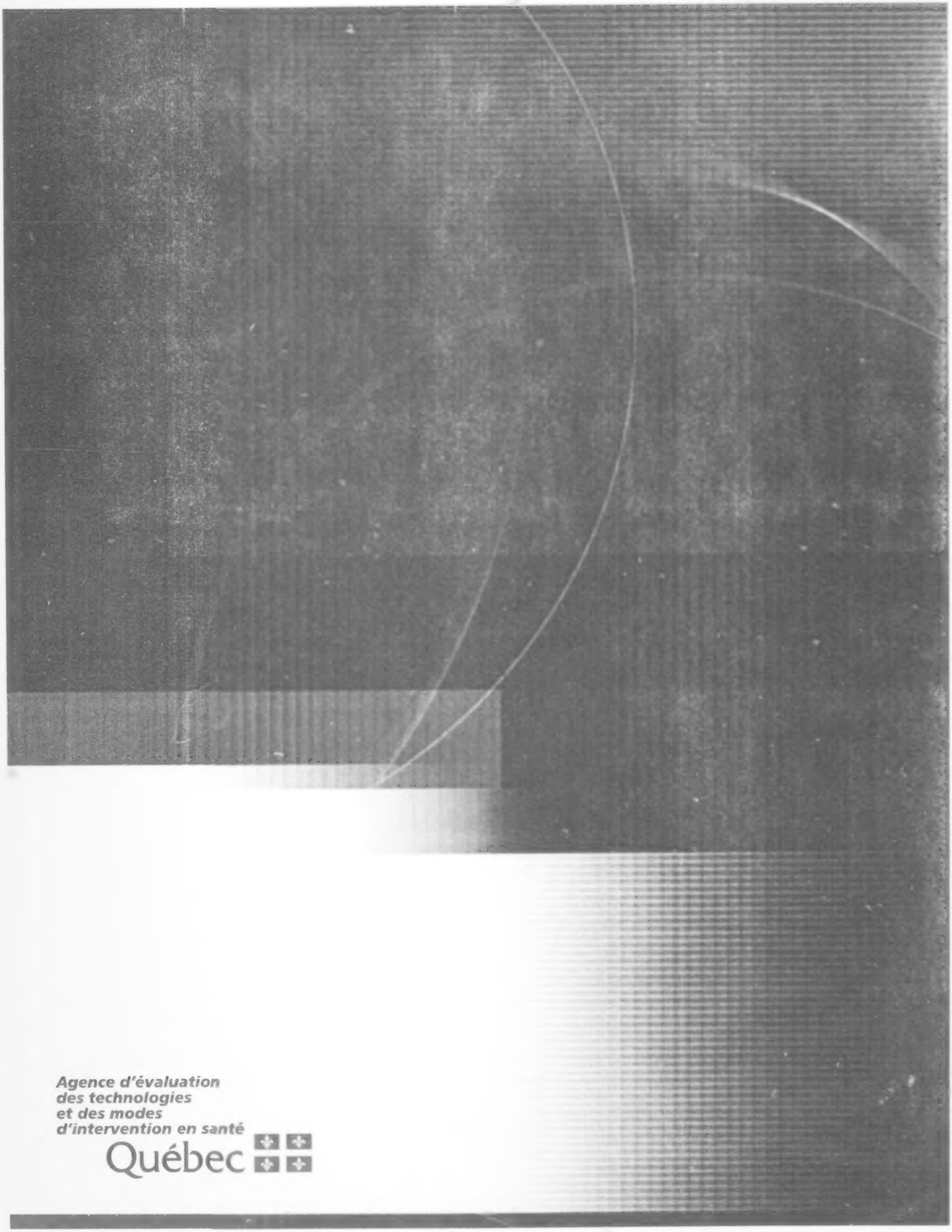
Weisberg M, Goldrath MH, Berman J, Greenstein A, Krotec JW, Fronio L. Hysteroscopic endometrial ablation using free heated saline for the treatment of menorrhagia. J Am Assoc Gynecol Laparosc 2000;7:311-6.

Wirz C, Gerber S, Genolet PM, De Grandi P. Clinical results with the Cavaterm™ thermal balloon endometrial ablation technique for the treatment of menorrhagia. In: Hohl MK, Dequesne J, Eberhard M, editors. 7th Congress of the European Society for Gynaecological Endoscopy; December 6 to 9, 1998; Lausanne, Switzerland:21-5.

Working Party for Guidelines for the Management of Heavy Menstrual Bleeding. An evidence-based guideline for the management of heavy menstrual bleeding. N Z Med J 1999;112:174-7.

Wortman M, Daggett A. Hysteroscopic management of intractable uterine bleeding. J Reprod Med 1993;38:505-10.

Yin CS, Wei RY, Chao TC, Chan CC. Hysteroscopic endometrial ablation without endometrial preparation. Int J Gynaecol Obstet 1998;62:167-72.



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